Subject Index to Volume 9

A Accommodation
Changes of ciliary region and ciliary zonule in (Araki) 150
Objective record of refractive changes due to (Harada et al) 189
Amaurotic
Idiocy: retinal arterioles in a case of (Matsusaka) 115
Amblyopia
Ex anopsia: Experiments on vision of (Adati) 22
Strabismic: Essential character and pathogenesis of (Harada) 1
Studies on (Uemura) 12
Aqueous
Rate of flow of (Shimizu) 28
Ascorbic
Acid: in Various tissues of eye (Shimizu) 68
C Cataract
Experimental Study on neutron induced (Choshi) 123
Ciliary
Region: in accommodation (Araki) 150
Corneal
Clouded: Angular distribution of light scattered from (Kinoshita et al) 48
Heterograft: Replacement of globulin fraction in (Itoi et al) 174
Nerve: Canals and less-myelinated nerve fibers (Wakui et al) 136
Nerve: Canals and less-myelinated nerve fiber bundles (Wakui et al) 199
Nerve: Constitution of (Wakui et al) 129
Stoma: on Water and cation shift of (Hara) 161
Stoma: Swelling and uptake of radioactive sulfate in (Sato) 92
Sodium-potassium-activated adenosine triphosphatase in (Maeda et al) 195
E Electron
Microscopic: Studies on zonule of bird and mouse eyes (Fukai) 80
Microscopic: Studies on juvenile amaurotic family idiocy (Matsusaka) 115
Microscopic: Observation on Sodium-Potassium-Activated Adenosine Triphosphatase in the rat cornea (Maeda et al) 195
ERG
Influence of pressure on (Usami) 108
of Oguchi's disease (Kubota) 31
G Glaucoma
Mass-screening: with water Provocative test (Chonan et al) 53
Glia
Cells: Histochemical studies on active transport ATPase of (Mizuno) 101
H Hypertensives
Comparative studies on retinal arteriolar and renal arteriolar changes in (Irinoda et al) 36
K Keratoprosthesis
Elastic (Itoi et al) 146
L Lens
Long-Term cultures of epithelial cells of (Tamura) 177
O Oguchi's disease

Studies on ERG of (Kubota) 31

P Presbyopia

Studies on (Kajiura) 85

R Refractive

Change: due to accommodation (Harada et al) 189

S Spielmeyer-Vogt

Retinal arterioles in a case of Juvenile Amaurotic Family idiocy (Matsusaka) 115

Strabismic

Amblyopia: Essential Character and Pathogenesis of (Harada) 1

T Tonography

Rate of flow of the aqueous by Suction and (Shimizu) 28

Tonometry

Anelasticity of eye ball and errors in (Itoi et al) 61

Trachoma

Virus: on developing chick embryo (Matsuda) 181

Z Zonule

Electron microscopic studies on (Fukai) 80

in Accommodation (Araki) 150

Index of Authors to Volume 9

A ADACHI Koichi: Some Experiments on the Vision of Amblyopia ex Anopsia 22
AKIYAMA Taichiro: see ITOI (2) 146
ARAKI Minoru: Changes of the Ciliary Region and the Ciliary Zonule in Accommodation 150
C CHONAN Tsuneo: Mass-screening of Glaucoma with Water Provocative Test 53
CHOSHI Kanji: Experimental Study on Neutron Induced Cataracts 123
F FUKAI Kiyoshi: Electron Microscopic Studies on the Zonule of Bird and Mouse Eyes 80
H HARA Tsutomu: Studies on the Water and Cation Shift of the Stored Cornea 161
HARADA Masami (1): Essential Character and Pathogenesis of Strabismic Amblyopia 1
(2): Objective Record of Refractive Change due to Accommodation 189
HASEBE Hisashi: see ITOI (3) 174
I IRINODA Kimiho: Comparative Studies on the Retinal Arteriolar and the Renal Arteriolar Changes in Hypertensives, as Studies by means of Ophthalmoscopy and Renal Biopsy 36
ITOI Motokazu (1): Anelasticity of Eye Ball and Errors in Tonometry 61
(2): Elastic Keratoprosthesis (Preliminary Report) 146
(3): Replacement of Globulin Fraction in Corneal Heterograft 174
K KAJIURA Mutsuo: Studies on Presbyopia 85
KANEKO Hiroshi: see ITOI (1) 61
KIKKAWA Yoshizo: see KINOSHITA 48
KINOSHITA Atsushi: Angular Distribution of the Light Scattered from the Clouded Cornea 48
KOMATSU Shinya(1): see ITOI (2) 146
(2): see ITOI (3) 174
KUBOTA Nobue: see HARADA 189
KUBOTA Yasuo: Studies on ERG of Oguchi's Disease 31
M MAEDA Kazumi: Studies on Sodium-Potassium-Activated Adenosine Triphosphatase in the Cornea
Electron Microscopic Observations on the Rat Cornea 195
MANABE Rizo: see KINOSHITA 48
MATSUDA Hidehiko: Culture of Trachoma Virus on Developing Chick Embryo (Report XII) 181
MATSUSAKA Toshihiko: Retinal Arterioles in a Case of Juvenile Amaurotic Family Idiocy (Spielmeyer-Vogt) 115
MATSUYAMA Shuichi: see IRINODA 36
MIZUNO Katsuyoshi: Histochemical Studies on Active Transport ATPase of the Glia Cells 101
N NIWA Yasuo: see ITOI (2) 146
O ONO Hiromitsu: see CHONAN 53
OZAWA Tetsuma: see HARADA (2) 189
S SAKAGUCHI Kazuyuki: see MAEDA 195
SATO Kiyotaka: Swelling and Uptake of Radioactive Sulfate in the Rabbit Corneal Stroma after Removal of Epithelium or Endothelium 92
SHIMIZU Hiroyuki: Intake and Distribution of Ascorbic Acid in Various Tissues of the Eye 68
SHIMIZU Koichi: The Rate of Flow of the Aqueous by Tonography and Suction 28

SUGIMACHI Tsuyomi: see ITOI (1) 62
SUGIURA Seiji (1): see WAKUI (1) 129
(2): see W. .KUI (2) 136
(3): see WAKUI (3) 199
T TAMURA Shigehiko: Long-Term Cultures of Epithelial Cells of a Rabbit Lens 177
TANDA Ikuko: see ITOI (3) 174
U UMEMURA Yasuo: Studies on Amblyopia 12
USAMI Emiko: The Influence of the Pressure on ERG of a Rabbit, Especially on A-wave and Oscillatory Potential 108
W WAKUI Kaichi (1): Constitution of the Corneal Nerve Canals 129
(2): Corneal Nerve Canals and the Less-myelinated Nerve Fibers 136
(3): Corneal Nerve Canals and the Less-myelinated Nerve Fiber Bundles 199

1

JAPANESE JOURNAL OF OPHTHALMOLOGY

VOLUME 9

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JAPANESE JOURNAL OF OPHTHALMOLOGY

VOLUME 9, 1965

Contents

Essential Character and Pathogenesis of Strabismic Amblyopia .....*Masami Harada*... 1

Studies on Amblyopia .....*Yasuo Uemura*... 12

Some Experiments on the Vision of Amblyopia ex Anopsia .....*Koichi Adachi*... 22

The Rate of Flow of the Aqueous by Tonography and Suction ..... *Koichi Shimizu*... 28

Studies on ERG of Oguchi's Disease .....*Yasuo Kubota*... 13

Comparative Studies on the Retinal Arteriolar and the Renal Arteriolar Changes in Hypertensives, as Studies by Means of Ophthalmoscopy and Renal Biopsy.....
.....*Kimiho Irinoda & Shuichi Matsuyama*... 36

Angular Distribution of the Light Scattered from the Clouded Cornea.....
.....*Atsushi Kinoshita, Rizo Manabe & Yoshizo Kikkawa*... 48

Mass-screening of Glaucoma with Water Provocative Test.....*Tsuneo Chonan & Hiromitsu Ono*... 53

Anelasticity of Eye Ball and Errors in Tonometry .....*Motokazu Itoi, Hiroshi Kaneko & Tsuyomi Sugimachi*... 61

Intake and Distribution of Ascorbic Acid in Various Tissues of the Eye.....
.....*Hiroyuki Shimizu*... 68

Electron Microscopic Studies on the zonule of Bird and Mouse Eyes.....
.....*Kiyoshi Fukai*... 80

Studies on Presbyopia .....*Mutsuo Kajiura*... 85

Swelling and Uptake of Radioactive Sulfate in the Rabbit Corneal Stroma after Removal of Epithelium or Endothelium .....*Kiyotaka Sato*... 92

Histochemical Studies on Active Transport ATPase of the Glia Cells.....
.....*Katsuyoshi Mizuno*...101

The Influence of the Pressure on ERG of a Rabbit, Especially on A-wave and Oscillatory Potential .....*Emiko Usami*...108

The Inclusion and the Intermitochondrial Bridge Appearing in the Retinal Arterioles in a Case of Juvenile Amaurotic Family Idiocy (Spielmeyer-Vogt).....
.....*Toshihiko Matsusaka*...115

Experimental Study on Neutron Induced Cataracts .....*Kanji Choshi*...123

Constitution of the Corneal Nerve Canals .....*Kaichi Wakui & Seiji Sugiura*...129

Corneal Nerve Canals and the Less-myelinated Nerve Fibers.....*Kaichi Wakui & Seiji Sugiura*...136

Elastic Keratoprosthesis (Preliminary Report).....*Motokazu Itoi, Taichiro Akiyama, Shinya Komatsu & Yasuo Niwa*...146

Changes of the Ciliary Region and the Ciliary Zonule in Accommodation.....*Minoru Araki*...150

Studies on the Water and Cation Shift of the Stored Cornea .....*Tsutomu Hara*...161

Replacement of Globulin Fraction in Corneal Heterograft.....*Motokazu Itoi, Ikuko Tanda, Shinya Komatsu & Hisashi Hasebe*...174

Long-term Cultures of Epithelial Cells of a Rabbit Lens .....*Shigehiro Tamura*...177

Culture of Trachoma Virus on Developing Chick Embryo (Report XII).....*Hidehiko Matsuda*...181

Objective Record of Refractive Change due to Accommodation.....*Masami Harada, Tetsuma Ozawa & Nobue Kubota*...189

Studies on Sodium-Potassium-Activated Adenosine Triphosphatase in the Cornea
Electron Microscopic Observations on the Rat Corneal .....*Kazumi Maeda & Kazuyuki Sakaguchi*...195

Corneal Nerve Canals and the Less-myelinated Nerve Fiber Bundles.....*Kaichi Wakui & Seiji Sugiura*...199

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no.1

1965 Vol. 9 No. 1

JAPANESE JOURNAL OF
OPHTHALMOLOGY

Contents

Essential Character and Pathogenesis of Strabismic Amblyopia ..... *Masami Harada*

Studies on Amblyopia..... *Yasuo Uemura*

Some Experiments on the Vision of Amblyopia ex Anopsia ..... *Koiti Adati*

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.....*Atsushi Kinoshita, Rizo Manabe & Yoshizo Kikkawa*

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Contents

Essential Character and Pathogenesis of Strabismic Amblyopia .....*Masami Harada*... 1

Studies on Amblyopia.....*Yasuo Uemura*...12

Some Experiments on the Vision of Amblyopia ex Anopsia .....*Koiti Adati*...22

The Rate of Flow of the Aqueous by Thnography and Suction .....*Koichi Shimizu*...28

Studies on ERG of Oguchi's Disease.....*Yasuo Kubota*...31

Comparative Stdies on the Retinal Arteriolar and the Renal Arteriolar Changes in Hypertensives, as Studies by means of Ophthalmoscopy and Renal Biopsy .....
.....*Kimiko Irinoda & Shuichi Matsuyama*...36

Angular Distribution of the Light Scattered from the Clouded Cornea.....
.....*Atsushi Kinoshita, Rizo Manabe & Yoshizo Kikkawa*...48

ESSENTIAL CHARACTER AND PATHOGENESIS OF STRABISMIC AMBLYOPIA

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The reduced visual acuity in the squinting eyes is not always due to an adaptive mechanism for strabismus but sometimes due to an invisible congenital impairment or an uncorrected ametropia if present. Therefore, in the strict meaning of the term, strabismic amblyopia should be named only on the case where reduced vision is closely connected with strabismus itself.

In most previous papers, however, little effort has been made to distinguish the true strabismic amblyopia from other kinds of amblyopia and there might have been occasions to mix up the cases with organic or anisometropic amblyopia in the materials of the studies. Under the circumstances, there still remain some questions on the problems of strabismic amblyopia.

It is the purpose of this study to know the essential character of strabismic amblyopia under the accurate diagnosis and to discuss the pathogenesis thereof.

Type of Fixation in Strabismic Amblyopia

The patients, associated with strabismus and amblyopia,were divided into two groups according to the location of fixation in amblyopic eyes: (1) central fixation group and (2) eccentric fixation group.

In a series of 62 cases, aged between 6 and 20 years, central fixation was observed only in 13 cases (20.9%) and remaining 49 cases showed eccentric fixation. A remarkable difference was noticed between two groups in the status of hypermetropic anisometropia (Table 1).

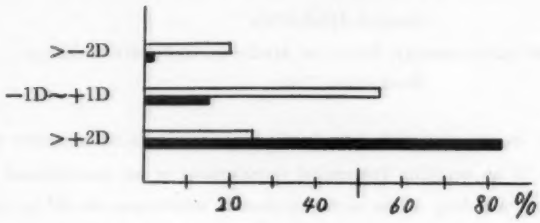
Table 1. Status of Hypermetropic Anisometropia in Centrically and Eccentrically Fixing Amblyopes

Hypermetropic anisometropia	With strabismus		Central fixation without strabismus
	central fixation	eccentric fixation	
Exist	10cases (76.9%)	6cases (12.3%)	28cases (77.8%)
Not-exist	3cases (23.1%)	43cases (87.7%)	8cases (22.2%)
Total	13cases (100%)	49cases (100%)	36cases (100%)

In the central fixation group, hypermetropic anisometropia was found in 10 cases (76.9%) of 13 cases and this percentage was almost equal to that in the cases of centrically fixing amblyopia without strabismus (77.8%). In the eccentric fixation group, on the contrary, hypermetropic anisometropia was observed only in 6 cases (21.3%) out of the 49 patients.

The distribution of the refraction anomalies in the amblyopic eyes was also different between two groups (Fig. 1). The majority of the centrically fixing amblyopes, with and without strabismus, had hypermetropia over 2 D. In the eccentric fixation group, however, hypermetroia over 2 D was not observed so frequently as in the former group, and this distribution had little specific significance compared

Fig. 1. Difference between central and eccentric fixation group in the distribution of refraction anomalies of amblyopic eyes.
Black line: central fixation amblyopia.
White line: eccentric fixation amblyopia.



with that of ordinary people of the same ages in this country.

From these studies, the followings may be concluded:

(1) Centrically fixing amblyopia is closely connected with higher hypermetropia especially with hypermetropic anisometropia even in the cases associated with strabismus and may bot be regarded as strabismic amblyopia.

(2) Eccentric fixation is the essential character of strabismic amblyopia.

There are some exceptions in the above conclusions; for example, cases of centrically fixing amblyopia without hypermetropia. The exceptional cases, however, were a few and could be diagnosed as organic amblyopia from the following precise examinations.

These conclusions were already confirmed by the author in his report[2] from another point of view.

Accommodation in Strabismic Amblyopia

The refractometer was used in an experimental examination of the amblyopes with eccentric fixation to observe how they accommodate themselves on the objects.

The method is shown in Figure 2. The refractometer is placed in front of the sound eye to test its refraction. At the same time, the test target is fixed at 1 m before the amblyopic eye. The target is then approached nearer to the eye until 30 cm. When the amblyopic eye has normal function of accommodation, the refractive power of the sound eye, which is tested by the refractometer,will increase for approximately 2.5 D according to the conjugate accommodation. However, if the amblyopic eye makes little effort of accommodation, hardly any increase of refractive power in the sound eye will be observed.

Fig. 2. The method of testing the accommodation of the amblyopic eye by observing the change of refractive power of the sound eye.

In order to know the function of the sound eye, the test can be made by placing the refractometer before the amblyopic eye.

The results of the experiment are shown in Table 2. In case of the patients with strabismic amblyopia, normal augmentation of accommodation according to the approach of the target was observed under the sound eye fixing; however, hardly any augmentation was observed under the amblyopic eye fixing. After the pleoptic treatment, the amblyopic eye possibly became to augment its accommodation equally to the sound eye.

Table 2. Augmentation of Accommodation according to the Approach of the Test Target from 100 to 30cm.

Fixing eye	Augmentation of accommodation	Visual acuity	Fixation
Sound eye	2.5D	1.2	Central
Strabismic amblyopia	(—)	0.06	Eccentric
Strabismic amblyopia (After treatment)	2.5D	0.4	Central
Macular degeneration	2.5D	0.08	Eccentric
Central scotoma due to retrobulbar neuritis	2.0D	0.1	Eccentric

In case of the patients with eccentric fixation caused by the organic disturbance, such as macular degeneration or retrobulbar neuritis, the augmentaion of accommodation according to the approach of the target was found almost normal in spite of their lower visual acuity and eccentric fixation.

The above results suggest that strabismic amblyopes do not accommodate themselves on the objects under the amblyopic eye fixing and this is an important character of strabismic amblyopia, which differs from organic amblyopia with similar eccentric fixation. Therefore this test is useful for the differential diagnosis of amblyopia. In case of bilateral eccentric fixation, for example, normal augmentation of accommodation was observed and this case was determined as organic amblyopia although there was little visible change in the fundus.

Electromyographic Analysis of Amblyopia

The technical development in electromyography has enabled us to record the discharges of the single neuromuscular unit continuously from the extraocular muscle when the patient is fixing a small test object at a considerable distance from his eye[5]. The disposition of the single unit discharges may indicate the situation of the centrifugal impulses on the extraocular muscles for maintaining the steady fixation.

The fixation movement of amblyopic eyes was already studied by Hayashi[6], von Noorden[8] and others. They confirmed the motor impairment of the amblyopic eyes by means of cinematography or electroophthalmography. The electromyographical analysis may have an advantage to know the characteristics of the fixation mechanism of amblyopic eyes especially in a very short time.

Method

An electrode needle was inserted into the external rectus muscle of the amblyopic eye of the patient, who was lying on his back and looking at a circular object of 5mm diameter at the distance of 40 cm from his eye, and the single unit discharges were recorded by a long recording camera. The speed of film movement was 20 cm per second. When one eye was fixing the target, the other eye was occluded.

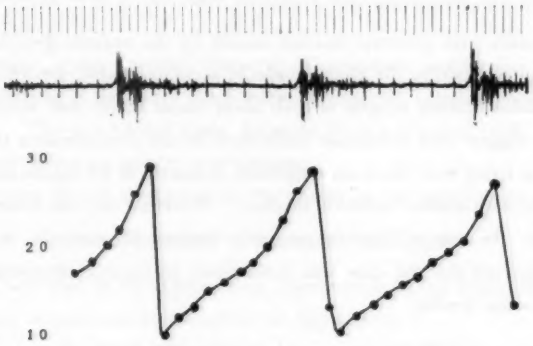
Results and Comments

In order to analyse the single unit discharge pattern, the interval diagram was produced, in which each interval between two successive discharges was plotted regularly. At first, the interval diagram obtained from the cases with nystagmus will be shown to facilitate understanding.

1. Nystagmus

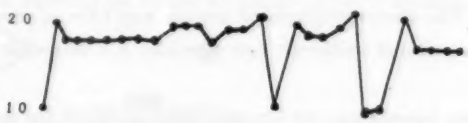
Figure 3 shows the record of single unit discharges and the interval diagram obtained from a case with eccentric nystagmus whose visual acuity is 0.5. The interval between two successive discharges becomes gradually longer, followed by a sudden onset of shortening of the interval. Each interval, measured in msec., is plotted regularly on the diagram wherein a recurrent fluctuation may be clearly observed. Although the fluctuation of the intervals is marked fully between 10 to 30 msec., it is not a confused one. A recurrent regularity is characteristic and it may indicate the controlled centrifugal impulse to maintain the clearer vision by overcoming the forced anomalous movement of the eyeball.

Fig. 3. Record of single unit discharges and interval diagram obtained from a case with eccentric nystagmus. Time scale: 10 msec.



In latent nystagmus, the interval diagram becomes quite different (Fig. 4). There are not rhythmical changes but irregular onsets of the shortening of the interval and quick recoveries from them. From this diagram, a regulating mechanism of maintaining the stable discharge pattern against the uncontrollable sudden shortening of the interval is recognized, and it may be understood that the visual acuity of this case is fairly good (0.7).

Fig. 4. Interval diagram obtained from a case with latent nystagmus.

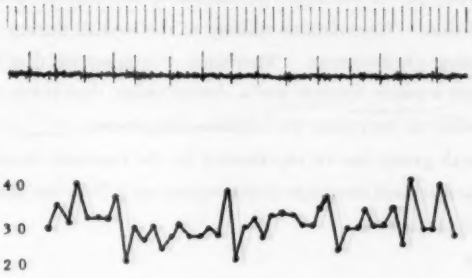


2. Organic Visual Disturbance with Eccentric Fixation

Figure 5 shows the record of single unit discharges and the interval diagram obtained from the eye with eccentric fixation caused by the monocular traumatic macular atrophy. Visual acuity is 0.04.

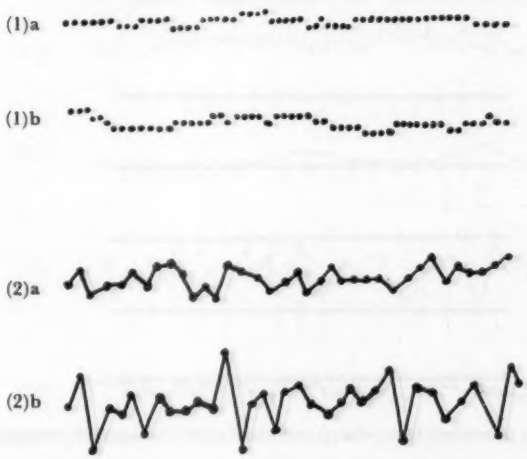
The disposition of single unit discharges is quite irregular and a remarkable fluctuation is observed in the interval diagram.

Fig. 5. Record of single unit discharges and interval diagram obtained from the eye with eccentric fixation due to monocular traumatic macular atrophy.



The fluctuation of the interval diagram is composed of two kinds of patterns: (1) small irregular group which is manifested in a very short time and (2) slow undulation which occurs in a relatively longer spun of time. The former is riding on the latter. These two can be separated by the method of moving averages. Figure 6 shows the slow undulation and the small irregular group in this patient

Fig. 6. Diagram of slow undulation and of small irregular group, produced from the interval diagram in the case shown in Figure 5.
(1): slow undulation. (2): small irregular group.
(a): sound eye. (b): affected eye with eccentric fixation due to traumatic macular atrophy.



under the affected eye fixing comparing with those under the sound eye fixing. A remarkable difference between the two may be seen in the small irregular group. An excessive irregularity is characteristic under the affected eye fixing. Once a considerable elongation of the interval occurred, it is immediately

adjusted by a successive shortening of the interval and therefore an excessive zig-zag fluctuation is produced. Such an adjusting phenomenon in a very short period of time has hardly been demonstrated by means of electrooculography. Owing to the organic lesion, the affected eye might be unable to maintain the stable fixation. This unstable fixation movement would not correspond to the marked irregularity in the diagram of small group but to the larger fluctuation in the diagram of slow undulation during the relatively longer period of time. Unavoidable shifting of the eyeball during the fixation may be minimized by the rapid adjusting phenomenon. Therefore, it is suggested that the affected eye does not abandon any effort to maitain a steady fixation and a clearer vision, but it has more or less a compensating adjusting mechanism in effect to overcome the organic disturbance.

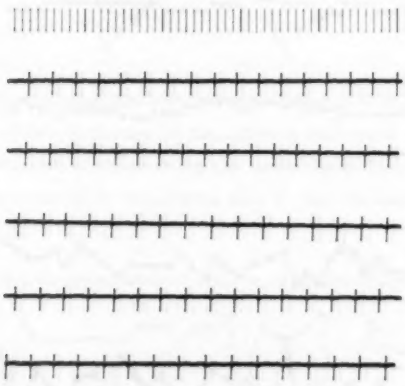
The irregularity of small group can be represented by the standard deviation of successive discharge intervals. In this case, the standard deviation is determined as 3.75 in the affected eye fixing pattern and 1.25 in the sound eye fixing pattern.

3. Strabismic Amblyopia

In strabismic amblyopia, it will be expected that more marked fluctuation may be recognized in the interval diagram because of the motor impairment of the amblyopic eye. However, an unexpected result was obtained.

The record of single unit discharges, obtained from a case with strabismic amblyopia under amblyopic eye fixing, is shown in Figure 7. In spite of the diminished visual acuity (0.02) and the loss of the central fixation in this case, single unit discharges are regularly disposed. It should be noticed, however, that this record is obtained in a relatively short period of time (2.5 sec.).

Fig. 7. Record of single unit discharges obtained from a case with strabismic amblyopia under amblyopic eye fixation. Recording continues from up to down.



The interval diagram, produced from this record is shown in Figure 8 comparing with that of the sound eye fixing. In the diagram of slow undulation, which may indicate the wandering of the fixation movement in a relatively longer period, a wider fluctuation is observed under the amblyopic eye fixing. In the diagram of small irregular group, however, an unexpected stability is seen under the amblyopic eye fixing.

Fig. 8. Interval diagram of slow undulation and of small irregular group obtained from a case with strabismic amblyopia.
(1): slow undulation. (2): small irregular group.
(a): sound eye. (b): amblyopic eye.

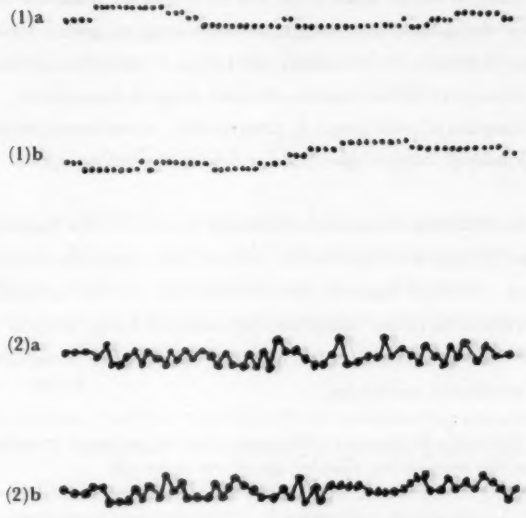
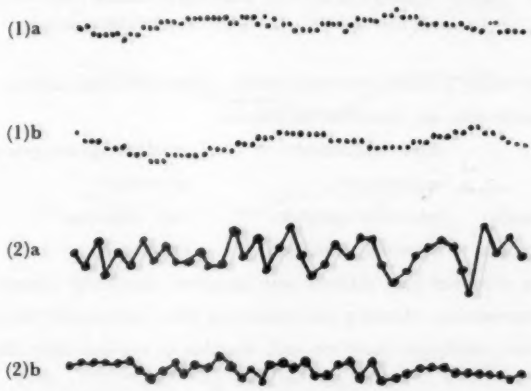


Fig. 9. Comparison between organic visual disturbance and strabismic amblyopia by interval diagram.
(1): slow undulation. (2) small irregular group.
(a): macular degeneration. (b): strabismic amblyopia.



If the amblyopic eye possessed a compensating adjusting mechanism to prevent the wandering of the fixation movement, the pattern of small group might have shown a zig-zag fluctuation as observed in case of organic visual disturbance. Little irregularity of small group would indicate that the amblyopic eye has no reaction to regulate its discharges against the gradual change of the intervals corresponding to the slow undulation.

This consideration may be confirmed by comparing the interval diagram of strabismic amblyopia with that of organic visual disturbance in another case. In Figure 9, the interval diagrams obtained from another case of strabismic amblyopia and from a case of macular degeneration are shown. Although the respective visual acuity is almost equal (0.06 and 0.08) and the fixation is similarly peripheral eccentric in these cases, neither the slow undulation nor the small irregualr group shows a quite similarity with each other in the interval diagram. In strabismic amblyopia, a wider fluctuation of the diagram of slow undulation and a less irregularity of the diagram of small group is recognized.

Little irregularity of the diagram of small group is characteristic in strabismic amblyopia and it seems to be the manifest results of lacking the feed back mechanism in the psycho-optical system of the amblyopic eye.

Table 3 shows the standard deviation of successive discharge intervals in the diagram of small irregular groups obtained from the cases of strabismic amblyopia, with reduced vision due to organic lesions, and of normal eye with normal vision. A larger standard deviation indicates a more irregularity. In all cases, the electromyography is recorded to have the mathematical mean discharge interval of about 30 msec., and this is important to know the significance of the obtained data. Little irregularity may be clearly recognized in every case of strabismic amblyopia.

Table 3 Standard Deviation of Successive Discharge Intervals in Small Irregular Groups (Figures in the brackets are years of age of the materials)

Normal eye	Strabismic amblyopia	Organic visual disturbance
1.55 (6)	1.24 (8)	1.84 (8) Retrobulbar neuritis
1.72 (8)	1.41 (14)	2.44 (11) Optic nerve atrophy
1.25 (16)	1.33 (17)	2.64 (12) Macular degeneration
1.41 (18)	1.10 (17)	1.87 (14) Macular degeneration
1.04 (21)	1.51 (18)	3.75 (17) Macular atrophy

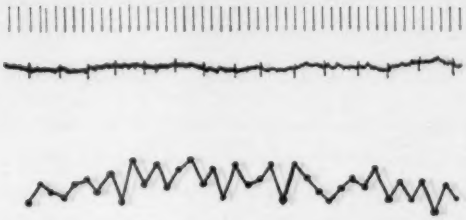
To sum up, differences among normal eyes with normal vision, eyes with organic visual disturbance and eyes with strabismic amblyopia are described as follows:

eyes	slow undulation	small irregular group
normal	uncommon	uncommon
organic disturbance	relatively common	very common
strabismic amblyopia	extremely common	uncommon

From these results, it is presumed that subjects with acquired monocular organic disturbance have a considerable degree of compensating adjusting mechanism in effect even under the affected eye fixing. While subjects with strabismic amblyopia have no such reaction to regulate their discharges under the amblyopic eye fixing.

From the practical point of view, the electromyographical analysis of disturbed vision may be useful for differential diagnosis of amblyopia. The reduced vision, without visible lesions, would be able to be analysed whether it is due to organic or functional disturbance. Figure 10 shows an example of such a differential diagnosis. The patient had the eccentric fixation and the central scotoma in the squinting eye whose visual acuity was 0.08. In this case, it was difficult to ditermine the correct diagno-

Fig. 10. Record of single unit discharges and interval diagram obtained from a case with eccentric fixation and central scotoma in squinting eye.

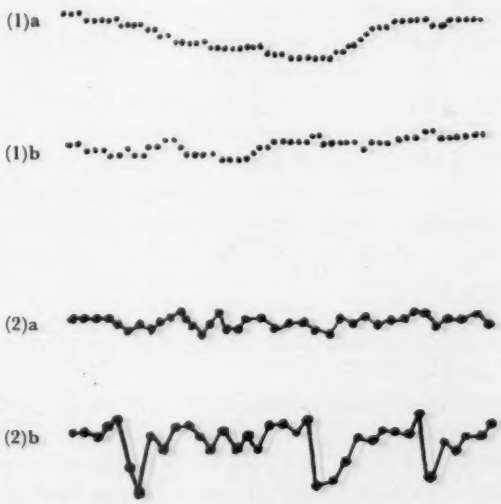


sis because there was no demonstrable change in the fundus corresponding to the central scotoma. The interval diagram,however, showed a considerable fluctuation and the patient was diagnosed as an organic amblyopia. No effect of peopltics was actually observed in this case.

Various kinds of nystagmus, especially latent nystagmus, may be sometimes misbelieved as the unsteady fixation movement of the strabismic amblyopia. They can also be diagnosed accurately by the electromyographycal analysis.

In strabismic amblyopia, it will be expected that the interval diagram will be different under the pleoptic treatment. Figure 11 shows the interval diagram obtained from a case with strabismic amblyopia before and after the treatment. By the treatment, the visual acuity is improved from 0.04 to 0.6. In this Figure, however, the diagram corresponds to a stadium in the course of treatment when the fixation is almost central and the visual acuity is 0.2.

Fig. 11 Interval diagram obtained from a case of strabismic amblyopia before and after treatemnt.
(1): slow undulation. (2): small irregular group.
(a): before treatment. (b): after treatment.



The remarkable slow undulation becomes rather stable by the treatment; while the small group becomes to have the marked irregularity by the treatment. The change of the pattern by the treatment would suggest the improvement of the compensating adjusting mechanism, because the pattern after the treatment would resemble to that of the organic disturbance or of the latent nystagmus.

Pathogenesis of Strabismic Amblyopia

The above studies revealed that the essential characters of strabismic amblyopia are (1) eccentric fixation, (2) no effort for accommodation and (3) no reaction to regulate the centrifugal impulses on the extraocular muscles for maintaining the steady central fixation. Of course, eccentric fixation is the manifest result of (3). These three characters may coincide with the defect of the motor component in psycho-optical reflex, i.e., the defect of the psycho-optomotor-reflex. Although they are frequently likend to the phenomena of "without attention" to the object[1], the patients have never abandoned their attention to the object. They have a volition to obtain the best visual acuity even under the amblyopic eye fixation and they know a way to maintain the steady fixation or the correct accommodation with the sound eye. The psycho-optomotor-reflx has to be manifested in both eyes simultaneously. Therefore, it is incomprehensible why such a reflex is defective only in one eye.

There are some patients, however, who have an abnormal psycho-optomotor-reflex acting separately to each eye under a certain condition. They are the cases of alternating hyperphoria. In these cases, each eye can be turned upwards by shutting off the light to the eye. Most cases of alternating hyperphoria are associated with manifest horizontal strabismus and when these patients are examined by synoptophore, an interesting phenomenon may be observed: the strabismic eye moves monocularly upwards and downwards by successive switching on and off the light of the target before the strabismic eye while the fixing eye is looking to the lighting target. The electromyography, recorded from the inferior oblique muscle of the squinting eye, indicates the active monocular movement of the eye, because the dischrages are observed to be increased or decreased according to switching off or on the light. This monocular shifting phenomenon is considered to be the evidence of an abnormal psycho-optomotor-reflex to one eye, and it may be regarded as a kind of primitive visual function as seen in the lower animals, in which each eye has a peculiar psycho-optomotor-reflex, i.e., a primitive monocular vision.

If strabismic amblyopia is considered to be a kind of such primitive monocular vision, every phenomenon would be easily understood. The psycho-optomotor-reflex manifests itself normally in one eye and abnormally in the other eye. The author already reported[3] that anomalous correspondence was considered as a kind of primitive monocular vision, however, it may be the sensory phenomenon in the visual space. Although there are essential differences among strabismic amblyopia, alternating hyperphoria and anomalous correspondence, they have a common nature as the primitive monocular vision. Therefore, it would be persuaded that there are some cases associated with strabismic amblyopia, alternating hyperphoria and anomalous correspondence.

Moreover, the above consideration would be supported by the changeover phenomenon[7]: alternation of the amblyopic eye by the sound eye occlusion.

The author recognized such a phenomenon in three infants with strabismic amblyopia, in which the sound eye lost its fixation after the several days occlusion while the amblyopic eye obtained the steady central fixation and became to be a fixing eye. For the occurrence of the changeover phenomenon, only several days occlusion was necessary. Therefore, neither the suppression nor anomalous correspodence in-

fluenced. Moreover, the occlusion of one eye occasionally provokes strabismic amblyopia to infants without strabismus. The author experienced a case of infant who became strabismus and amblyopia after the several days' occlusion of one eye by the treatment of corneal ulcer. In this case, both strabismus and amblyopia seemed to occur at the same time because the loss of fixation in the strabismic eye was found when the occlusion was removed.

These facts suggest that the previously reported theories about the development of strabismic amblyopia, such as the suppression theory etc., are doubtful because the amblyopia with eccentric fixation does not develop in the specially-fixed eye, like the strabismic eye, but in one eye unaffected by strabismus. It would be considered that the occlusion of one eye leads the primitive monocular vision which would be the cause of either strabismus or amblyopia. Therefore, strabismic amblyopia should not be regarded as the result of strabismus.

The problem as to the cause of eccentric fixation has not been satisfactorily solved yet. From the electromyographical analyses, it seems to be clarified that the fixation behavior of eyes with strabismic abmlyopia is not consistent with that of the organic amblyopia. An active feed-back mechanism, to overcome the organic disturbance for maintaining the better vision, is commonly observed in the latter. However, such a feed back mechanism is never found in the former. Strictly speaking, the eccentric fixation in strabismic amblyopia can not be regarded as the behavior of fixation, because hardly any fixation reflex is accompanied with. The amblyopic eye is only opening towards the object with a lack of the psycho-optomotor-reflex. Therefore, it is natural that a fixed eccentric fixation point is never recognized in the fundus and the location of fixation area is easily shifted after the strabismus operation. The amblyopic eye is able to direct its foveal region to the object after the proper strabismus operation without any pleoptic treatment.

Moreover, the author has already reported that the visual acuity of the foveal region of the amblyopic eye is not so diminished but is rather better as compared with that of the eccentric fixation area[4]. These phenomena would also be the counter-evidence against the formerly believed theories upon the origin of eccentric fixation.

According to the above facts, the term of eccentric fixation is not suitable and the term of loss of fixation will be recommended.

As the treatment of strabismic amblyopia, a simple occlusion has a considerable effect especially in early childhood. The primitive monocular vision would easily develop in younger children and accordingly the easy recovery from it would be expected also in early childhood. The recommendation of early treatment may be based on this reason.

Summary

The statistical and experimental studies were performed to clarify the essential and the pathogenesis of strabismic amblyopia. The results brought us the following conclusions:

(1) The essential of strabismic amblyopia is considered to be the primitive monocular vision characterized by the defect of the psycho-optomotor-reflex in one eye.

(2) Strabismic amblyopia would not be the result of the strabismus of long duration. A common cause, such a primitive monocular vision, may provoke both strabismus and amblyopia simultaneously.

(3) Eccentric fixation is the main character of strabismic amblyopia, however, it is not considered

as the behavior of true fixation because the lack of the psycho-optomotor-reflex. The term of loss of fixation is recommended.

(4) Centrically fixing amblyopes can not be regarded as strabismic amblyopia even when they are associated with strabismus. They must be determined either as anisometropic amblyopia, if higher hypermetropia is observed in the amblyopic eyes, or as organic amblyopia by the precise examinations.

The objective examination of accommodation by the refractometer and the electromyographical analysis by producing the interval diagram of the single unit discharges are available for clarifing the nature of the visual disturbances of various cause and solving the problems upon amblyopia.

REFERENCES

1. Balen, A.T. and Henkes, H.E.: Brit. J. Ophth., 46; 12, 1962.
2. Harada, M. and Hayashi, S.: J.J.O., 2: 268, 1958.
3. Harada, M.: J.J.O., 1: 73, 1957.
4. Harada, M. and Yamamoto, H.: J.M.P.A., 55: 238, 1961.
5. Harada, M. and Maruo, T.: J.C.O., 18: 329, 1964.
6. Hayashi, S.: Acta O.Jap., 64: 679, 1960.
7. Scully, J.: Brit. M. J., 5267: 1610, 1961.
8. von Noorden, G.K.: Am. J. Ophth., 53: 642, 1962.

STUDIES ON AMBLYOPIA

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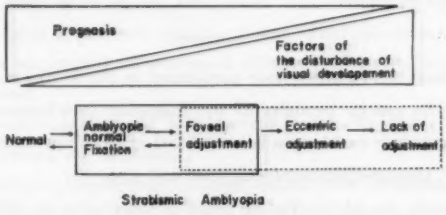
Amblyopia may be defined as decreased vision which cannot be explained by organic pathologic changes. Through the years our knowledge of the physiopathology of amblyopia has slowly increased, a great deal still remains obscure.

I presented the following hypothesis: Amblyopia may be established by the disturbance of visual conditioning or abnormal conditioning during the visual development process. The congenital or acquired factors in early childhood which disturbed the vsual development were not simple, but were omplicated one. The amblyopes were serious and poor prognosis of these factors were more complicated (Fig.1).

The various factors of the disturbance of visual development as follows:

Fig. 1. Diagramatic representation of the distribution of strabismic amblyopia.



1) Sensoric factors

(1) Primary

(a) Congenital anomaly
(b) Accident at birth
(c) Diseases in early childhood
(2) Secondary (influence by motor anomaly)
(3) Other factors
(a) Refractive error
(b) Psychologic factor-nervous instability
(c) Intelligence
(d) Attitude of learning

2) Motoric Factors
(1) Primary
Strabismus (comitant, paralytic)
(2) Secondary
(a) Deteriorated primary motor anomaly
(b) Influence by sensoric change
(3) Other factors
(a) Refractive error
(b) Psychologic factor

Fixation Reflex Test

The new method for the fixation behavior examination, fixation reflex test, was evaluated by using pleoptophore. It has been known that the central fovea has its maximum visual function in the retina by positioning the image of an external objects. This was done if the system employs a signal proportional to displacement of the image from the fovea and controls the movement of the eye in such way as to reduce this discrepancy to zero. This feature represents the essential behavior of a position control servo with negative positional feedback. The fixation reflex which was one of optovotro reflex was a closed servo loop in the feedback mechanism. The purpose of the fixation reflex test was the investigation the abnormal state with optomotor reflex in the strabismic amblyopia.

Methods

After checking the fixation behavior, this test was carried out by the examiner while the fundus was under direct observation through the telescope of the pleoptophore. By moving the fixation object on good eye, spot light stimulation was carried out at each retinal regions (nasal, above, temporal and below retina from macula) by turns in the fellow eye. In the healthy eye, we observed eye movement which was to bring rapidly and acurately fovea to the light spot as shown as Fig. 2.

By the new method, the amblyopes with abnormal fixation, which were detected by visuscope before, were classified as follows: (1) foveal adjustment (2) eccentric adjustmnt (3) lack of adjustment (Fig.3).

Results and comments

The results of fixation reflex test in 82 of the cases with fixation's anomaly were as shown in Table 1. In exotropes, the cases of eccentric adjustment were mostly demonstrated, on the contraly,the cases of

Fig. 2.

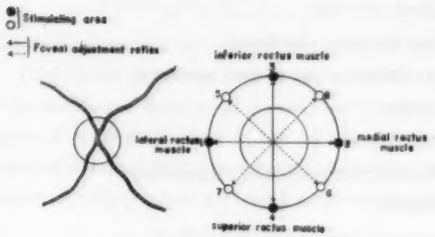


Table 1. Fixation Reflex Test (82 cases of Eccentric fixation)

FRT \ Squint	Exodeviation	Esodeviation	Total
Foveal adjustment	1 (6.6%)	28 (41.8%)	29 (35.3%)
Eccentric adjustment	10 (66.7%)	22 (32.8%)	32 (39.0%)
Lack of adjustment	4 (16.7%)	17 (25.4%)	21 (25.7%)
Total	15	67	82

foveal adjustment were mostly in esotropes.

The relation between fixation reflex test and fixation behavior was as shown in Table 2. It has been demonstrated that the more remoteeccentric area was from the fovea, this lack of motor and sensory mechanism became the more pronounded.

Table 2. The relation between Fixation Reflex Test and Fixation behavior

FRT \ Fixation	CF (H)	Pf. F.	Pm. F	P.F.	O.F.	Total	Total -CF(H)
Foveal adjustment	13 (30.9%)	16 (38.0%)	8 (19.0%)	5 (12.1%)	/	42 (40.4%)	29 (35.3%)
Eccentric adjustment	/	1 (3.1%)	12 (37.5%)	19 (59.4%)	/	32 (33.6%)	32 (39.0%)
Lack of adjustment	/	/	1 (4.8%)	13 (61.9%)	7 (33.3%)	21 (26%)	21 (25.7%)

(1) The feature of the cases with foveal adjustment were as follows.

(a) Use of fixation point situated extrafoveal area by the results of visuscope examination but, foveal adjustment were noticed by light stimuli with this test (Fig. 3).

(b) Mazuda color filter VR63 was used. When the diagnosis for the eccentric fixation has been made, the healthy eye was fully patched and the amblyopic eye coverd with the red filter. We have observed in many cases that the fixation shifted to the fovea as soon as the red light was used for substitution of the white light (Fig. 4).

(c) The visual acuities on the fovea and the eccentric area were compared by the pleoptophore under the direct ophthalmoscopy. The visual acuity was better on the fovea than the eccentric area (Fig.5).

(d) After the test treatment by pleoptophore, central fixation may be restored and the visual acuity im-

Fig. 3. Fixation reflex test.

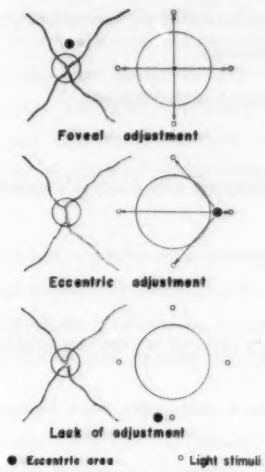


Fig. 4. Red filter test.

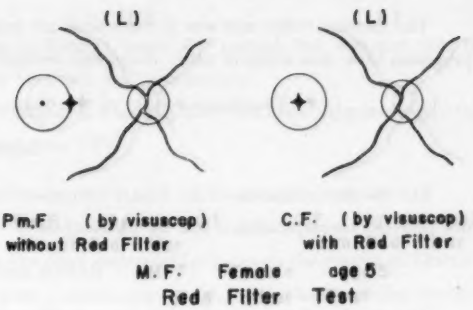
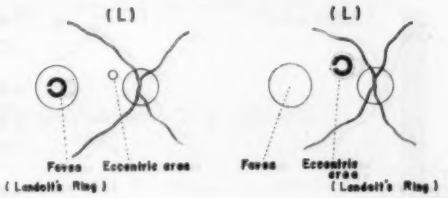


Fig. 5. The comparative measurement of visual acuity between fovea and eccentric area under observation of fundus, using pleoptophore.



proved temporaly.

(e) Pleoptics were the most effective method for restoring central fixation and for the visual improvement.

(2) The feature of the cases with eccentric adjustment were as follows:

(a) The large eccentricity was vastly more frequent in patients who showed eccentric adjustment.

(b) The shifting of fixation's point from eccentric area to fovea has not occured by use of red filter.

(c) The visual acuity in eccentric area was better than or the same in fovea.

(d) Pleoptics were mostly ineffective in the cases with eccentric adjustment.

(3) The feature of the cases with lack of adjustment were as follows:

In these cases, any adjustment movement were not noticed by light stimuli. In cases with lack of adjustment, 31.6% have obtained foveal adjustment, 31.6% to eccentric adjustment and 36.8% were unchanged after pleoptic treatment. It must be pointed out, however, that 75% of the children between the age of 3 and 4 years have obtained normal fixation and improved visual acuity after pleoptic treatment in our experience. On the contraly, pleoptics was not effective for the children over 5 years of age.

Summary

The fixation reflex test was a more accurate guide to determination of the method of treatment and prognosis than was using of other diagnostic method such as visuscopy.

The Examination of the State of the Retinal Correspondence

Methods

For the determination of the retianl correspondence in an amblyope with fixation's anomaly, we used the bifoveal correspondence test by pleoptophore.

Results and comments

The results of the examination were as follows:
60% of esotropic amblyopes and 86.7% of exotropic amblyopes showed anomalous retinal correspondence (Fig. 6).

The types of anomalous retinal correspondence in strabismic amblyopes were vairous and were classified in four types (Fig. 7, Table 3).

Fig. 6. Frequency of abnormal retinal correspondence in strabismic amblyopia.

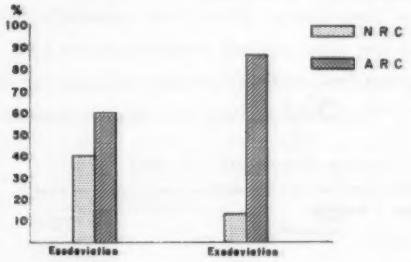


Fig. 7. Classification of retinal correspondence in strabismic amblyopia.

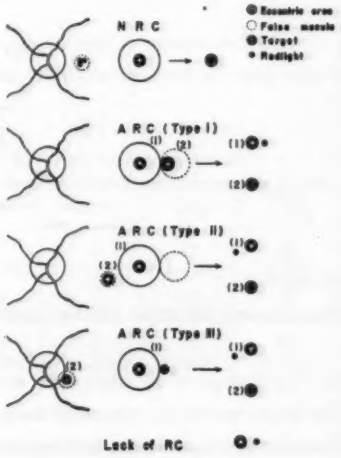


Table 3.

Classification \ Type of squint	Exodeviation	Esodeviation
NRC	2 (13.3%)	14 (40.0%)
ARC Type Ⅰ	6 (39.9%)	9 (25.7%)
ARC Type Ⅱ	4 (26.6%)	3 (8.6%)
ARC Type Ⅲ	0	3 (8.6%)
Lack of R.C.	3 (20.2%)	6 (17.1%)

ARC type I: in this type, the close relationship between eccentric fixation, "false macula" and ARC existed.

ARC type II: the close relationship between eccentric fixation and ARC existed, but was not able to demonstrate any rleationship between the angles of anomaly and eccentricity.

ARC type III: The close relationship between the angles of anomaly and ARC was demonstrated but, not existed any relationship between the eccentricity and ARC.

ARC type IV: the lack of retinal correspondence.

Summary

In this study, we have demonsrated that there are close relationship between the results of fixation reflex test and retinal correspondence but, in view of these complicaing results, it must be stated that correspondence hypothesis presented by Cüppers is most attractive and convincing, final proof for its validity for all cases of abnormal fixation has yet to be produced.

Pursuit Eye Movement

Pursuit eye movement was registerd using television eye camera. The mechanism of eye movement control and disturbances in strabismic amblyopia were studied, The results showed that the pursuit eye movement was normal under binocular viewing condition. However, the disturbance of pursuit movement was remarkable when the fixed eye was occuluded. Pursuit movement was demonsrated in Fig. 8 which may serve as a representative smaple.

Case S. K. age 27, female.

R- strabismic amblyopia

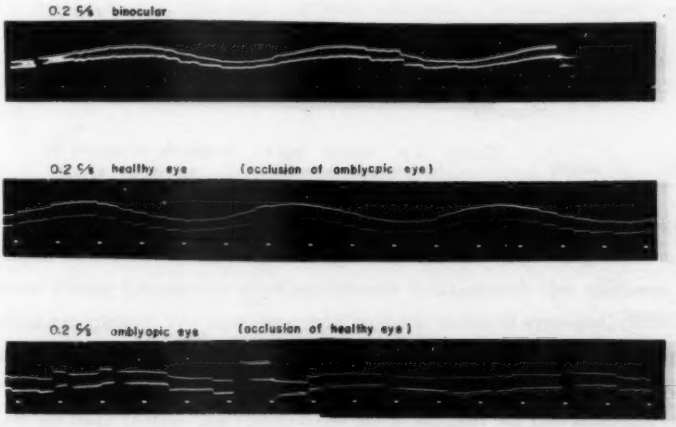
visual acuity O. D. 0.1, O. S. 1.2

eye position: -5°XT, Fixation behavior C. F. (hunting)

FRT: foveal adjustment

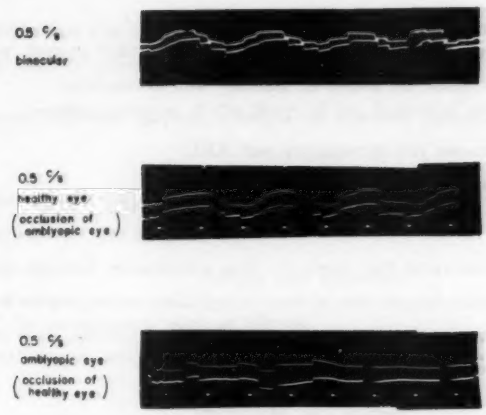
Fig. 8. Pursuit eye movement.

(a)



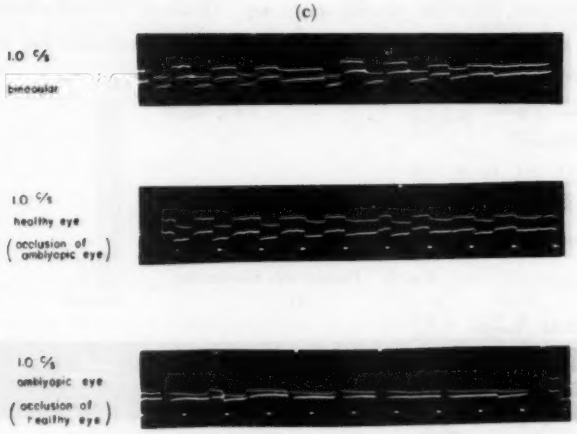
Case 5 S. K. female age 27 Strabismic Amblyopia (R)

(b)



Case 5 S. K.. female age 27 Strabismic Amblyopia (R)

(c)



Case 5 S. K. female age 27 Strabismic Amblyopia (R)

The average amplitude of a subject's response over many cycles was measured at various frequencies up to maximum of 1.0 cps. As shown in Fig. 8, sequence of curves obtained from healthy eye and binocular viewing condition was demonstrated smooth continous sine-shaped pursuit movement.

On the contrary, sequence of curves obtained from amblyopic eye (healthy eye occluded) was noted marked difference of behavior in comparison with healty eye: Eye movement was very discontinuous and irregular or disappeared.

These facts suggested that the response of the servo system was normal when the retinal information cause from healthy eye, but was instable or inactive when the information cause from the amblyopic eye.

Balint's Similar Syndrome

The similar symptoms were seen in amblyopes with abnormal fixation, like Balint's syndrome, especially optic ataxia.

(1) Tracing method

In our own experience, tracing method was available for the examination of hand eye coordination in an amblyope with eccentric fixation. Line drawing as shown in Fig. 9 were designed for the aid of diagnosis of eccentric fixation. Patient draw a line with a pointed red pencil following a line drawing. If patient had abnormal fixation, the results were showned in Fig. 10. These method were simple and good methods to decide the stadium to begine the treatment due to corrector and localisator.

Fig. 9. Tracing method.

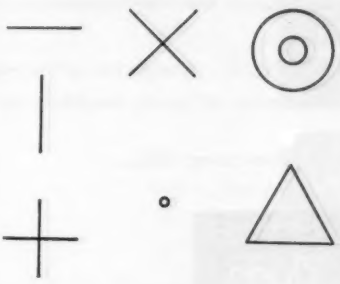
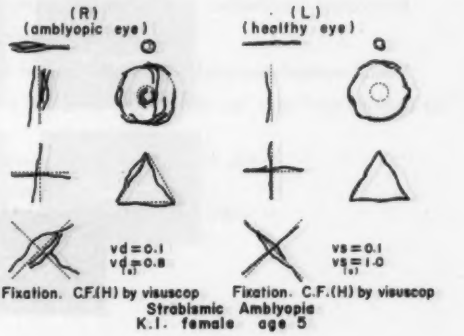


Fig. 10. Tracing method.



(2) When the patients were instructed to bind two points by line drawing, they could be done under healthy eye, but could not be done under amblyopic eye (Fig. 11).

(3) If the patient were orderd to draw triangle or circle, they could be done under healthy eye, but its forms were not completed using amblyopic eye as shown in Fig. 11.

However, the pathogenesis of these syndrome were unknown. Probably these occure in such cases.

Fig. 11. The examination of the recognition of the visual spatial sense.

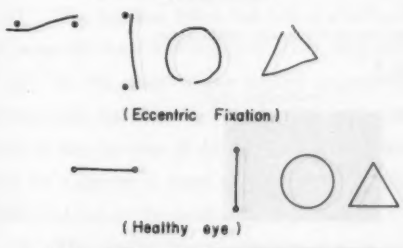
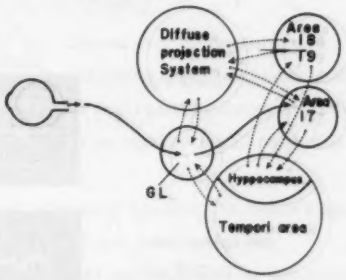


Fig. 12. To and fro connection in the central nervous system with conduction of visual information.



(a) A defect of sensory information to area 18 or 19 from 17 and insufficient development of visual engram.

(b) Insufficient development of the connection circuit from visual areas to temporal lobe.

(c) Insufficient development of to-and fro connection from cortex to subcortical (Fig. 12).

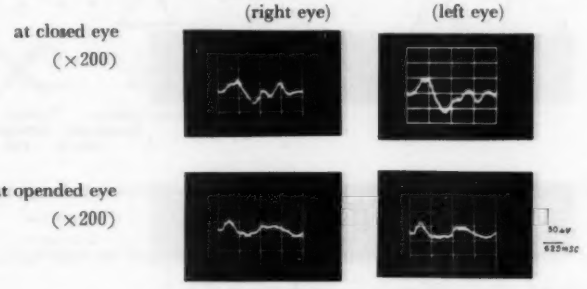
The Visual Evoked Potential in Amblyopes

Several experiments dealing evoked response of visual cortex in amblyopes were described in the literature. Van Ballen and Henkes (1962) used Dawson's superimposition method together with the mathematical integration method. In this study, we recorded the visual evoked potential using computer of average transcient, CAT. The CAT was a multi-purpose "on-line" computer. It has been successfully used for detection of evoked responses in the brain.

Recording conditions: energy of stimulator flash: 1/2V.C. distance from eye to stimulator: 40cm.
Background illumination: 30 lux.

Visual evoked potential in a normal person were as shown in Fig. 13. Comparison of the responses "at opened eye" and "at closed eye" revealed a change in the relation of latency amplitude and after

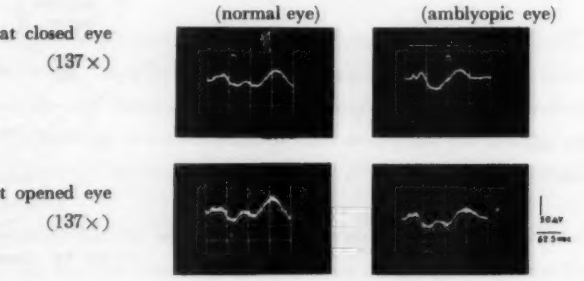
Fig. 13. Visual evoked potential in a normal person, using CAT.



discharge, but the responses of each eye under same condition were almostly same.

Visual evoked potential in strabismic amblyopia was demonstratedin Fig. 14 which may serve as a representative sample.

Fig. 14. Visual evoked potential in a patient from squint amblyopia.
K.S. female age 4



Case L.S. age 4, female

L-strabismic amblyopia

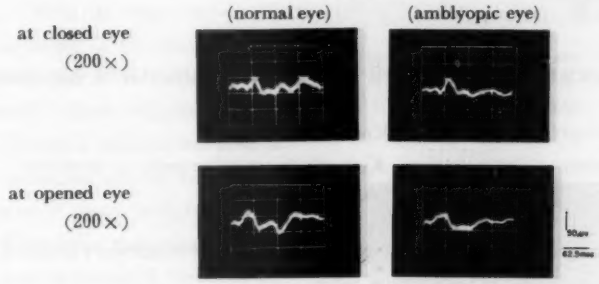
visual acuity O.D 0.8, O.S 0.1

fixation behavior: P.F. (visuscope) FRT: eccentric adjustment

Some change was observed in the responses between the eyes opened and closed. In strabismic amblyopes, responses to the same intensity of flash showed remarkable in the closed eye, but no remakable difference between the amblyopic and normal eye was observed.

Visual evoked potential in anisometropic amblyopia was demonstrated in Fig. 15.

Fig. 15. Visual evoked potential in a patient suffering from anisometropic amblyopia.
S.K. female age 10



Case S.K. age 10, male

L-anisometropic amblyopia

visual acuity O.D. 1.0 (id+0.5D) O.S. 0.05 (0.1+4.5D)

eye position: normal fixation behavior: C.F

In anisometropic amblyopes, the responses showed remarkable difference between the amblyopic and normal eye when the eyes were opened.

Summary

The pathophysiology of amblyopia with abnormal fixation has been studied by fixation reflex test, television eye camera and visual evoked potential. The following points have been stressed.

(1) The fixation reflex test was a more accurate guide to determination of the method of treatment and prognosis than was using of other diagnostic method such as visuscopy.

(2) In the study of the retinal correspondence uisng the bifoveal test by pleoptophore, we have demonstrated that there are close relationship between the results of fixation reflex test and retinal correspondence but, in view of these complicating results, it must ve stated that correspondence hypothesis presented by Cüppers is most attractive and convincing, final proof for its validity for all cases of abnormal fixation has yet to be produced.

(3) The similar symptoms were seen in amblyopes with abnormal fixation, like Balint's syndrome, especially optic ataxia. However, the pathogenesis of these syndrome were unknown.

(4) The problem of visual evoked potential in amblyopes could not be solved in this study.

REFERENCES

1. Bangerter, A.: Amblyopiebehandlung, ed. 2. Basel-New York, 1955.
2. Penfield, H.& Roberts L.: Speech and brain mechanisms, Pinceton, New Jersey, 1959.
3. Cüppers, C.: Schilen, Pleoptik, Orthoptik, Operation, 1, 1961.
4. Fender, D.H.& Nye, P.W.: Kybernetik, 2: 81, 1961.
5. Davson, H.: The Eye. vol. 1–4. Academic press, New York and London, 4. 1962.
6. Von Noorden, G.K.& Mackensen, G.: Am. J. Ophthal., 53: 642, 1962.
7. Haik, G.: Strabismus (Symposium of the New Orleans Academy of Ophthalmology) the C. V. Mosby company, 1962.
8. van Balen, A.T.M. & Henkes, H.E.: Brit. J. Ophth., 46: 193, 1962.
9. Uemura, Y.: Acta O. Jap., 66: 1097, 1962.
10. Uemura, Y.: Acta O. Jap., 68: 663, 1964.

SOME EXPERIMENTS ON THE VISION OF AMBLYOPIA EX ANOPSIA

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This is a report of several experiments to explain the nature of visual sense involved in amblyopia ex anopsia, the experiments being consisted of 3 parts:—

1. Experiment with fundus camera involving fixation targets, designed to elucidate the problem concerning disparity of monocular fixation (DMF).

2. Experiment on the spreading excitation of retina and brain in the patients with amblyopia ex anopsia.

3. Experiment on brain level of the visual function of amblyopia ex anopsia.

1. It is a current opinion to explain the cause of the eccentiric fixation by assuming an increase of visual ability in ARC point or on the margin of central inhibitory retina. However, we have many evidences to find the origin of the eccentric fixation in the deficiency of optomotoric reflex of amblyopia.

Eccentric fixation is a type of anomalous fixation confronted with the sequence of the counteraction between the fixation weakened by low visual acuity and the rest positioning of the squinting eye. It reveals itself in expanded form of DMF, which is an essential delay of fixation movement involved in the servo-mechanism of fixation in normal state[1 2].

Fig. 2. shows groups of pictures taken with the fundus camera, each group consisting of 3 different positions of the eye, one in the primary and two in the horizontal secondary, 30° apart from the primary, as is shwon in fig. 1.

In fig. 2 (A, B, C, D) is clearly shown that the improvement of fixation is brought about by squint operation and abnormal large DMF is markedly decreased by pleoptics, whereas the visual acuity remains unimproved, keeping neraly the initial value of 0.1.

Thus we have no way to estimate what the decreased DMF brngs about in his visual life, although some good influence is expected. Therefore it seems unreasonable to evaluate the effect of pleoptics only by measuring the visual acuity.

Patients with exotropia generally tend to show eccentric fixation with retinal points temporal to the fovea, but such as that in adducted position is not rare, probably being influenced by the elevated tonus of medial rectus muscle, which is brought about by cerebral attention, activated when the patient tries to fix an object with his eye of low visual acuity.

From these considerations, DMF seems not to hold in all cases of eccentric fixation as its essential origin. Thus its cause should be sought in the real depth of the visual sense.

2. For the analysis of the composition of visual acuity, Pavlov's theory of generalization, differenciation, irradiation and concentration of excitation and induction should be born in mind. The process of sharp inhibition to the marginal zone of spreading excitation will correspond to the process in which visual acuity forms itself. And this process may be the same as the process in which lateral inhibition is formed by adequate connection of neurons.

From this viewpoint, amblyopia is not the products of inhibition from the fellow eye via the cortex but the results of the lack of inhibition, necessary for the sharpness of the image in retina and brain.

a. Experiment to separation difficulty[5].

Separation difficulty means that, for example, the visual acuity with crowded E is lower than that with single E. But the acuity with crowded E provided with a circle aound the central E is unexpectedly higher than with that without a circle.

Fig. 1. Taking position of fundus camera. 1, 2, 3 corr. to 1, 2, 3 of fig. 2.

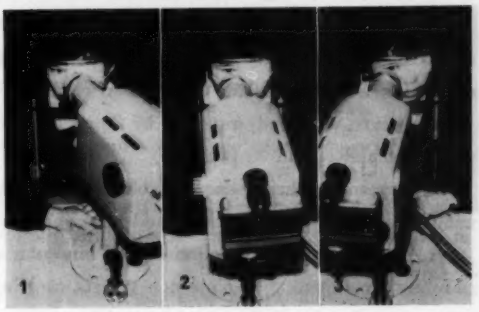
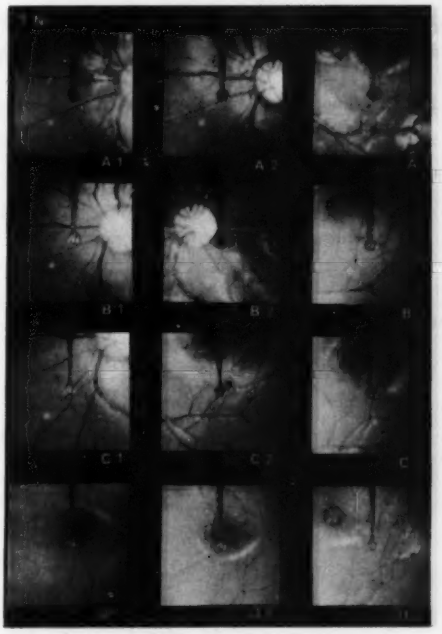


Fig. 2. Fixation point and DMF: Esotropia +28° (LV=0.05). A. before oper. B. after oper. C. 1 mon. pleoptics (LV=0.1). D. 3 mon. pleoptics, with improvement of DMF.



From those observations, it is assumed that the decrease of acuity in the separation difficulty is caused by the spreading disturvance from the surrounding Es towards the central E, and in amblyopia the spreading is so high that the phenomenon of the separation difficulty is marked.

b. Color sensation of amblyopic eye.

There is close relationship between Motokawa's induction theory and color vision, and some relation

between induction and spreading excitation is assumed to be in existence. So if the abnormal spreading of excitation exists there may be some influence on color sensation in amblyopic eye.

The tendency to deuteranomalia is chekced out by testing with pseudoisochromatic plates in 5 patients with eccentric fixation whose visual acuity range from 30 cm/n.d. to 0.2, while in 5 patients with normal flxztion (30 cm/n.d.–0.3) no sign of color anomaly is detected.

However, as already reported by Oppel[7], we cant' find out any kind of color anomaly by the tests with anomaloscope in all patients.

The peculiar phenomenon in color sense observed in eyes with eccentric flxation, Pigmentfarbenanomale reported by Heisnius[3], should be probably caused by some anomalous retinal function.

c. Analysis of the vision induced by binocular apparent movement. Fig. 3 shows my device adopted in my experiment. Two pin-hole targets, each hold differing in vertical position are inserted each into right and left tube of Stanworth's modified major amblyoscope with transparent head and alternate fiickerings (2.5 cps) to both tragets are given. In this situation, luminous spot is seen by the subject, moving up and down through the half mirror on the screen presented in front of him.

Apparent movement is described by Motokawa[6] as one of the phenomena related with the induction of Motokawa. And, following his theory, these binocular apparent movements are considered as the consequence of induction not in retina but in binocular area of brain.

Projecting the 3rd spot on the screen and covering one side of half mirror, we can get the central

Fig. 3. Binocular apparent movement and its central representation.

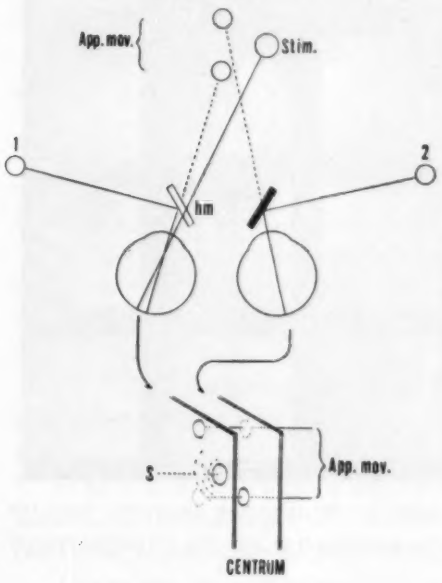


Fig. 4. Disturbance of app. mov. by spreading effect of stim. spot.
●: amblyopic
○: normal side in centrum.

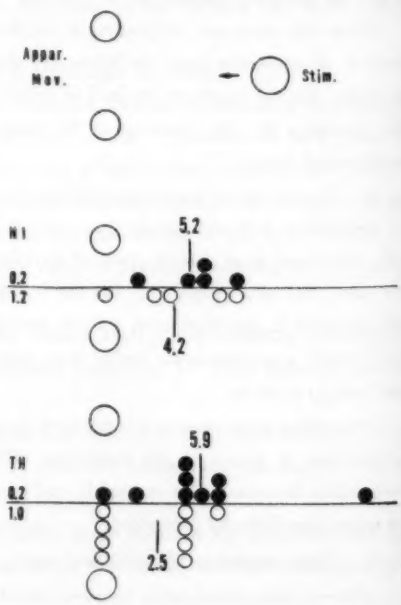


image (s. in fig. 3) to any side of centrum, normal side or amlyopic side.

Disturbence of apparent movement occurs when the 3rd stimulus come close to fiickering spots. It is very likely to consider that the more large the area of spreading excitation in brain the more wide the distance between the pair of spots and the 3rd stimulus on screen enough to bring forth the disturbance.

As shown in fig. 4 the 3rd spot on the amblyopic side disturbes the apparent movement with further distance from the target than that on the normal side.

This facts seems to tell us more large spreading of excitation around the neural image of the spot on amblyopic side of brain than on the normal side.

3. Recently, I have come to be aware of the existence of some qualitative differences between visual sensation of highly amblyopic eye and of normal or slightly amblyopic eye, an idea which has led me to carry out the next experiment.

In this experiment, a sensation of "ease", with which the subject sees the surroundings is used as the criterion.

To lower the visual acuity of the nonamblyopic eye in order to equalize the "ease" with that with the amblyopic eye, by loading with plus lenses, the acuity of the nonamblyopic eye does not need to be decreased so low as to be leveled to that of amblyopic eye. The acuity of 0.5–0.7 of the nonamblyopic eye corresponds, in the sensation of "ease", to that of the amblyopic eye, that is 0.1 or less.

However, in cases of slight amblyopia (visus 0.3 or more) or of visual insuffiency due to any organic disease, the visual acuity of the better eye is needed to be lowered to the level of the worse eye to equalize the "ease" (Fig. 5).

From the hypothesis of an existence of double centers for the visual sense, it is conceivable that with the development of the visual function of the infant. the connection of the retina with the lower center will be converted to that with the higher center (Fig. 6).

Fig. 5. Equalizing of visual "ease". Visual acuity of amblyopic eye (abscissa), decreased acuity of normal eye (ordinate).

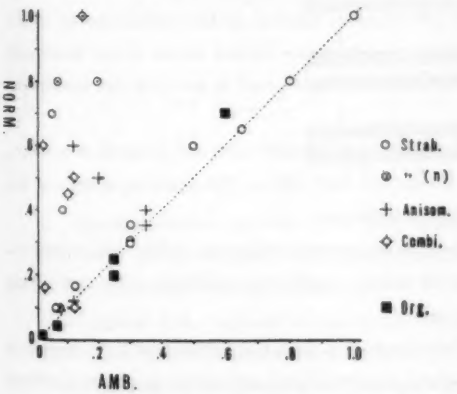
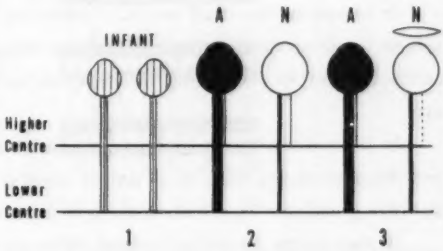


Fig. 6. Hypothetical double stage of visual centre corresponding to amblyopic and normal eye.



By cutting off the connection of the normal functioning eye with the higher visual center by lowering its visual acuity, the balance in the visibility between normal and amblyopic eye should be easily attained. On this point of view, the visual pattern of the amblyopic eye is to be considered as such maintaining the initial connection with the lower center.

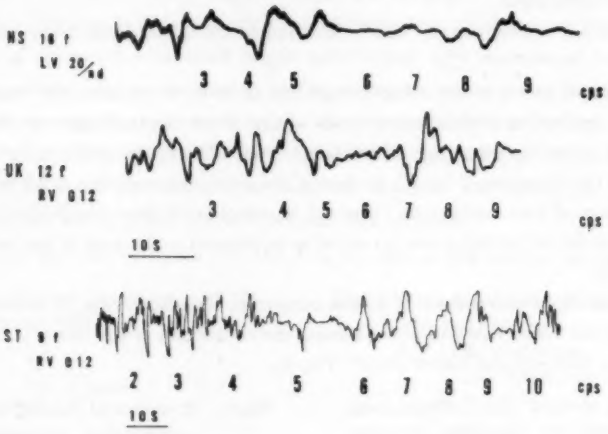
Assuming the θ-wave region of the brain as lower visual center, I have planned following experiments:–

a. Fixation nystagmus in the influence of flickering light.

Fixation nystagmus of amblyopic eye is observed by disposing the patient to 300 lux flickering light of variable frequency using EOG as recording method.

By changing the frequency of flicker, remarkable decrease of amplitude of nystagmus is observed just on the range of frequency of flicker equivalent to θ-wave (Fig. 7).

Fig. 7. Fixation nystagmus of amblyopic eye illuminated with flickering light of var. freq.



b. Visual acuity in the influence of flicker.

In measuring the visual acuity, it seems not to be apropriate to depend on the verbal answer of the subject to pic up the direction of Landolt's rings, because it needs higher central action of the brain and exerts difficulty for the unintegrated subjects, such as infants and those forced to see with the amblyopic eye.

In my experiment, chekerd patterns consisting of small dots of variable sizes are adopted as a chart, and the patients are required to answer whether he can see the each dot on the chart separately or not by reflex grasping rubber bulb in his hand connected to the indicator.

In these states, the patient's visual ability is conceived to lie between minimum visible and minimum separable, and this procedure with which a patient gives answer might be considered to be more tonic or protopathic one than with verbal or phasic response.

Fig. 8. shows the results of my experiments. The stimulation with 6 cps flickering light reveals in amblyopic vision a remarkable drop of visual acuity, and this phenomenon is never seen in vision of normal eye whose acuity is artificially depressed.

These facts have led me to the conclusion that the amblyopic vision holds more close connection with the lower center of brain than normals, and is therefore liable to be interfered with by flickering, corresponding to this level of brain.

Fig. 8. Visual acuity of amblyopic eye illuminated with flickering light.

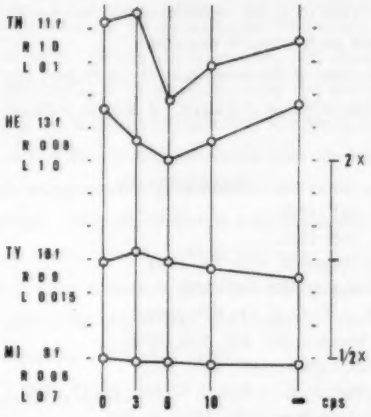
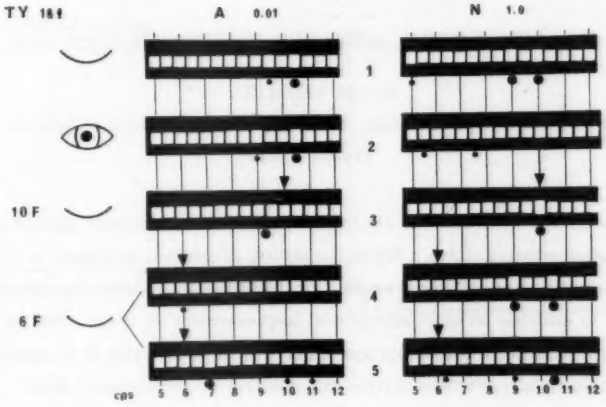


Fig. 9. Freq. spectra of EEG, when illuminated with flickering light (10, 6 cps.): ▼ driving freq., ● component freq.



c. Synchronization between EEG and flicker.

To verify the above mentioned asumption, EEG is tested if it synchronizes to the flickering, presented to the amblyopic and the fellow eye.

The applied EEG analyser is one of mechanical resonance type with pitch of 0.5 cps.

One of the results of experiment is shown in fig. 9.

The first part of the series is a EEG spectrum with closed eye, typical α-wave being illustrated.

The 2nd part of the series shows a pattern with open eye and α-blocking is lacking in amblyopic eye (A).

From this pattern it can be recognized that the vision of the amblyopic eye, as described by many authorities[8,9], is in a state of lack of attention.

In the 3rd part of the series, stimulations with 10 cps flicker are given to the normal eye and amblyopic eye. The stimulation to the normal side gives synchronization with EEG, but not the stimulation to amblyopic side. This facts have led us to the consideration that amblyopic eye might scarcely have connection with 10 cps-area of brain as Matteuci[4] described.

However in the 4th and 5th part of the series with 6 cps flicker, any positive proof for the connection of amblyopic eye to the 6 cps-area of brain is found. I believe further experimentation should be needed.

REFERENCES

1. Adati, K.: F. O. J. 12: 531, 1961.
2. Adati, K.: F. O. J. 12: 713, 1961.
3. Heinsius, E.: Klin. Mbl. Augenhk. 135: 95, 1959.
4. Matteuci, P.: Ophthalmologica 140: 81, 1960.
5. Matuda, M. and Adati, K.: F. O. J. 13: 334, 1962.
6. Motokawa, K.: J. Exp. Psychol. 45: 369. 378, 1953.
7. Oppel, O.: Greaefes Arch. Ophth. 165: 387, 1963.
8. Van Ballen, A. T. and Henkes, H. E.: Brit. J. Ophth. 46: 12, 1962.
9. Yuge, T.: Strabismus, Tokyo, Nanzando, 1963, p. 331.

THE RATE OF FLOW OF THE AQUEOUS BY TONOGRAPHY AND SUCTION

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Tonography has opened an era in our knowledge over the hydrodynamic aspects of intraocular pressure in normal and glaucomatous states. While the facility of outflow, expressed as C, has been taken to represent fairly well the true state of affairs implied by definition of the term, the rate of flow, expressed as F, has been subject to criticism in spite of repeated improvements in the method of calculation. The following is an attempt to ascertain the major sources of error of the F value in tonography through correlation with data obtained by perilimbal suction cup method in normotensive eyes.

Materials and methods

58 eyes of human subjects, who have been considered as nonglaucomatous upon reasonable clinical grounds, served as materials of the study. Routine tonography and suctioning with standardised perilimbal suction cup were performed upon the eyes at different days. Care was taken to make the two examinations within one week at the most and preferably at the same hour of the day. The table of Moses et al. was used for tonographic calculations and the value of 10 mmHg was assumed for the episcleral venous pressure in determining the value of aqueous flow. The duration of perilimbal suctioning at a vacuum of 50 mmHg was set either at 10 minutes or 15 minutes. The rate of flow was estimated from the difference in intraocular pressure before and after suctioning according to the table by Langham over the pressure-volume relationship for average human eyes in situ.

Results

The rate of flow obtained by suction is presented in Fig. 1 against the initial intraocular pressure as abscissa. When the suctioning continued for 10 minutes, the mean rate of flow was 1.36 mm^3/min with the standard deviation of 0.36 (N=12). When the suctioning was done for 15 minutes, a lower value was obtained, the mean rate of flow being 0.96 mm^3/min with the standard deviation of 0.41 (N=46). Although the number of the cases is too small to be subjected to a strict statistical analysis, it is seen from the figure that the value for the rate of flow is not correlated with the initial intraocular pressure.

The rate of flow obtained by tonography is presented in the same manner in Fig. 2 set against the initial intraocular pressure as abscissa. The rate of flow is seen to assume a value which increases in linear proportion to the initial intraocular pressure level. While the mean rate of flow (M=1.19) is of the same order as is obtained by suction, it is quite apparent that the similarity lies only in the average value and that, as concerns the pattern of distribution of the data, the results for the F value obtained by suction and by tonography are entirely incompatible with each other.

Fig. 1. Rate of flow of the aqueous by suction.
Ordinate: rate of flow per minute in cubic millimeters
Abscissa: initial intraocular pressure in mmHg
×: suction for 10 minutes
•: suction for 15 minutes

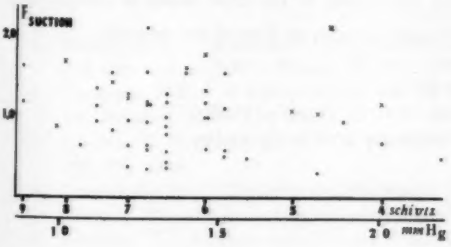
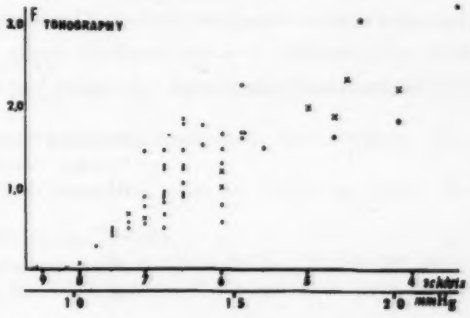


Fig. 2. Rate of flow of the aqueous by tonography.
Ordinate: rate of flow per minute in cubic millimeters
Abscissa: initial intraocular pressure in mmHg



Discussions and conclusions

The present tonographic data are in line with the findings of a previous paper of the author concerning the tonographic data on 200 eyes, which stated that, whereas the coefficient of outflow (M=0.27, s=0.09, N=200) was independent of the initial Po level, the value for the rate of flow stood in linear proportion to the initial intraocular pressure.

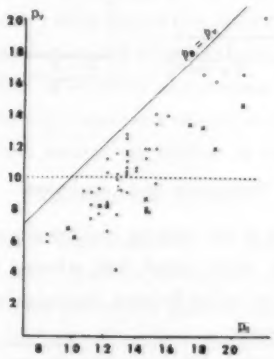
The tonographic method for calculation of the rate of flow has been subject to several criticisms, though, it must be admitted, great advances in ophthalmology have been brought about in the past through mediation of tonographic F value as, to take a few examples, in elucidating the hypotensive mechanism of carbonic anhydrase inhibitors or in establishing hypersecretion glaucoma as a minor but definite clinical entity. While the customary formula F=C (Po-Pv), a due consequence of Poiseiulle's law upon which tonography

is theoretically founded, seems to have been accepted in general, criticism has been directed at the assumption that the Pv, the episcleral venous pressure, is a constant at 10 mmHg based upon the unaminously confirmed data since Seidel through direct measurements. Several clinical findings have been reported which contradict the above assumption. Cases have been described in which active outflow of aqueous was present in aqueous veins in eyes with tensions of less than 10 mmHg. Another report stated that, in eyes recovering from extreme hypotension induced by compression, the flow of aqueous in the aqueous vein started when the intraocular pressure reached the level of 7.24 mmHg. It was Stepanik who proposed the value of 4 mmHg for the Pv value from quantitative determination of the rate of flow through cinematographic observations of the aqueous vein.

From the data of the present study it becomes possible to calculate in a retrograde fashion the Pv value using the formula $Pv = Po - F/C$, in which F stands for the rate of flow obtained by suction and C for the value by tonography. It is of course not to be assumed here that the thus obtained Pv stands for the absolute actual value. We can study, though, the general tendency of the Pv value in spite of certain inherent sources of error involved in the method.

It is apprently shown in Fig. 3, in which the calculated Pv value is plotted against the initial Po value, that the Pv is not a constant, but is a variant that changes parallel to the Po value at a pressure head (Po-Pv) of an average of 3 mmHg. It is further shown that in 26 out of 58 cases the Pv assumes a value of less than 10 mmHg. The first finding is an expected one if both the F and C values were independent of initial intraocular pressure. The second finding points to the inadequacy to set a rigid value for Pv at 10 mmHg. It is thus concluded that in these two points lie the chief causes of disagreement between tonography and suction cup method in determining the rate of flow of the aqueous.

Fig. 3. Estimated value for Pv
Ordinate: estimated value for Pv. ($Pv = Po - F/C$)
Abscissa: initial intraocular pressure in mmHg



Although the suction cup method is a recently developed one with numerous and not sufficiently explored sources of uncertainty, one can accept the saying of Ericson that the errors of the method are of systematic nature and that the obtained values for the apparent rate of flow tend to be less than real. It follows, therefore, that if the values for the rate of flow obtained by suction exceed those by tonography,

the former can be taken to represent better the actual values. Comparison of tonography and suction has thus shown the basic errors in hypothetical assumptions in tonography. It is further shown that, at least in normotensive eyes, the suction cup method can give decidedly more accurate values for the rate of flow than by tonography. The suction cup method is thus expected to supplement inherent defects in tonography.

Summary

A critical comparative study was attempted over the values of the rate of flow of the aqueous in 58 normal eyes by tonography and by suction cup method. While the F values obtained by suction stayed within a certain range independent of initial Po level, those by tonography changed in linear proportion to the Po value.

Analysis of basic principles for the suction cup method pointed to the tendency for the calculated F value to appear less than the actual and substantiated the assumption that the data for the F value obtained by suction are to be given preference over those by tonography in normotensive range, where both methods give conflicting results. Suction cup studies show that the relative hypotension often observed in normal eyes is not as a rule due to hyposecretion of the aqueous but to the extremely low episcleral venous pressure with undiminished aqueous secretion.

In 45% of the eyes studied the Pv value estimated from the rate of flow by suction and from the tonographic coefficient of outflow stood less than 10 mmHg with an average pressure head between the intraocular and episcleral venous presure of 3 mmHg.

LITERATURE

1. Ericson, L.A.: Twenty-four hourly variations of the aqueous flow. Examinations with perilimbal suction cup. Acta Ophth. Suppl. 50:1–95, 1958
2. Langham, M.E.: A new procedure for the analysis of intraocular dynamics in human subjects. Exp. Eye Research 2:314–324, 1963
3. Shimizu, K. & Kobayashi, K.: Tonographic data on normal eyes. Acta Soc. Ophth. Jap. Suppl. 68: 651–656, 1964
4. Leydhecker, W.: Glaukom ein Handbuch. 138–139, Berlin, 1960
5. Soeteren, T.: Aqueous flow in hypotonic and glaucomatous eyes. Acta Ophth. 38: 347–363, 1960
6. Soeteren, T.: Further investigations of aqueous flow in normal eyes after compression. Acta Ophth. 38: 496–510, 1960
7. Stepanik, J.: Die Tonographie. Fortschr. d. Augenh. 11: 119–251, 1961

STUDIES ON ERG OF OGUCHI'S DISEASE

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Only a few reports have been made on ERG in Ougchi's disease, but very few on ERG after lengthy dark adaptation. The retina of this disease has a pathologically peculiar scotopic mechanism. Therefore, as suggested by Jacobson[5], it will be very interesting to analyse the electroretinographic records on after long term dark adaptation of Ogudhi's disease.

The aim of this study is to investigate ERGs of a typical case of Oguchi's disease after lengnthy dark

adaptation as well as to analyze the mechanism of a_1-, a_2-waves.

Case

T.S., an 11 year-old boy, came to our clinic on August 1, 1963, mainly complaining of nyctalopia, which had been his trouble since his infancy. His parents were first cousins, but he seemed to have no hereditary defect.

Vision of his both eyes was normal under bright daylight, but very defective under dim light. Fig. 1 shows thr visual field of this case, in which the constriction was seen especially on a dim object.

Fig. 1. Visual field of the case of Oguchi's disease.

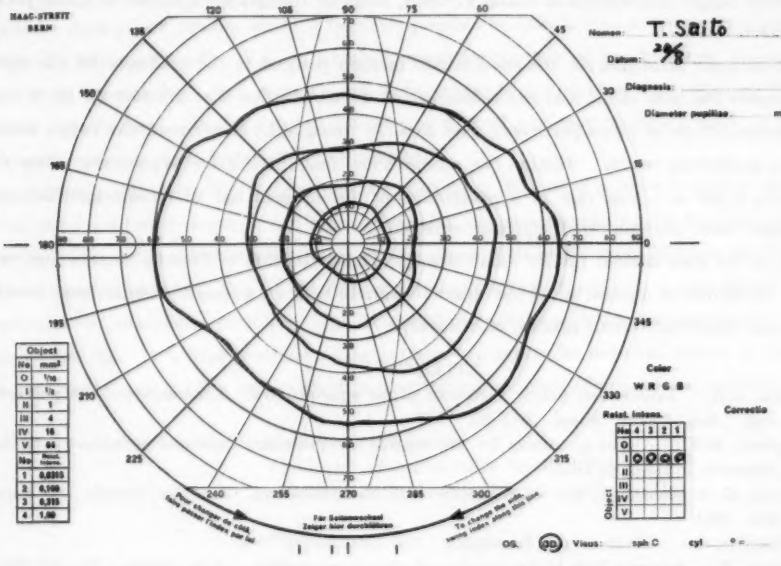
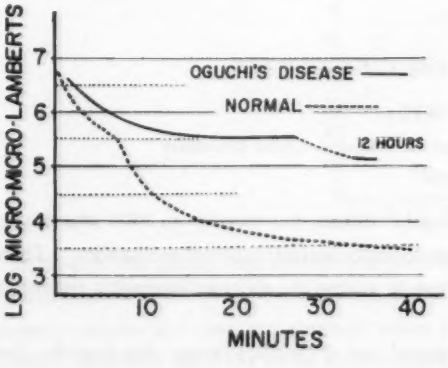


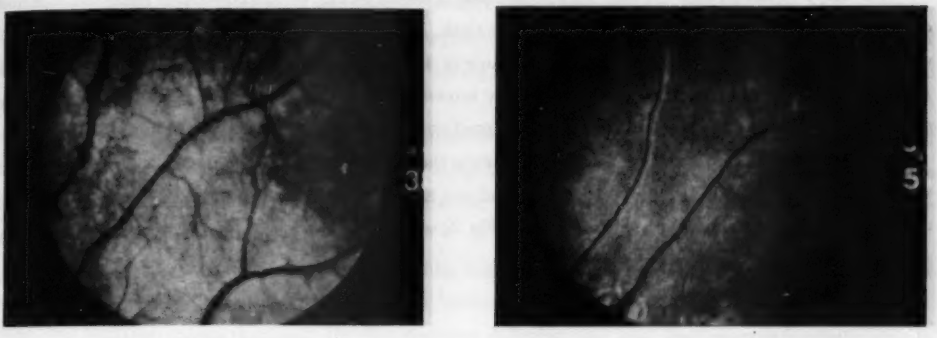
Fig. 2. Dark adaptation curve of the case of Oguchi's disease.



As to its dark adaptation curves, as shown in Fig. 2, there were disturbances both in the first and second curves. The external eye examination showed nothing abnormal; while the fundus examination revealed characteristic changes of the disease. The disc and the macula were normal. The posterior pole of the retina was almost normal, but specific yellowish phosphorescent discoloration was seen (Fig. 3) in the peripheral region of the retina.

Mizuo's phenomenon was clearly observed in the patient, and after 3 hours in the dark the color of the fundus peculiar to the disease took a normal appearance.

Fig. 3. Fundusphotographs of the case of Oguchi's disease. Before dark (left) and after 3 hours in dark.



Apparatus and Method

As a light stimulus of ERG, white flash from Xenon gas charge was used. The ERG was derived from Lo-Vac type contactlens electrode. After dark adaptation this corneal electrode was inserted under dim red light. The responses were led into an amplifier which activated the cathode ray oscillograph, and were recorded photographically.

Results

The ERG of a normal object after10 minutes in the dark is shown in Fig. 4. And Fig. 5 shows the ERG of the case of Oguchi's disease after the same 10 minutes in the dark. In the latter, the a-wave was nearly half in amplitude compared with that of the normal ERG, and several oscillatory potentials which followed the a-wave were clearly recognized.

Fig. 4. ERG in the normal subject after 10 minutes in dark. (Time mark: 100 msec. Calibration: 0.1 mV.)

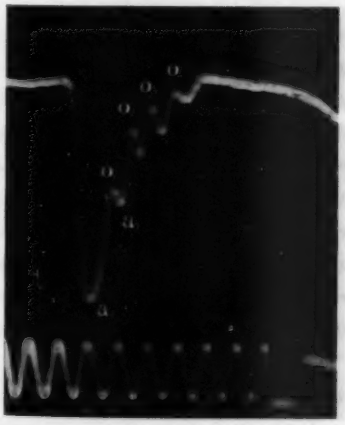
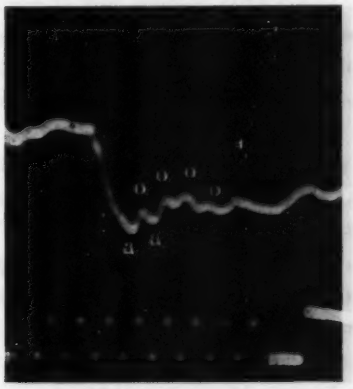


Fig. 5. ERG in the case of Oguchi's disease after 10 minutes in dark.



The b-wave was not observed. The first negative component (so-called a_1) was larger than the

second negative component (so-called a_2) in amplitude.

The ERG obtained after 3 hours dark adaptation is shown in Fig. 6. Such form of ERG was obtained only by the first light stimulus after 3 hours in the dark. Of course, the corneal electrode had been inserted under dim red light at that time. The amplitude of the a-wave enlarged and the b-wave also appeared. And the amplitudes of a_1-and a_2-waves were very interesting. The amplitude of a_1 was larger than that of a_2, and, moreover, the amplitude of this a_1 enlarged more than that of a_1 adapted 10 minutes in the dark.

Fig. 7 shows the ERG obtained after 12 hours in the dark. Also at this time, such form of the ERG was obtained only by these first light stimulus; and the ERG obtained by the second stimulus 10 minutes after the first one was the same as that shown in Fig. 5, when the fundus examination revealed still normal appearance as Mizuo's phenomenon.

Fig. 6. ERG in the case of Oguchi's disease after 3 hours in dark.

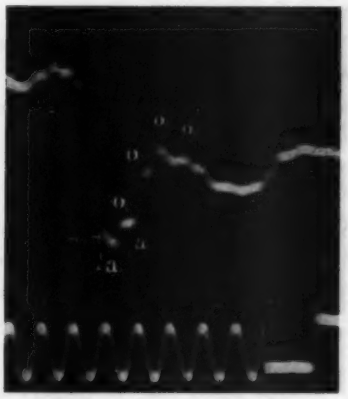
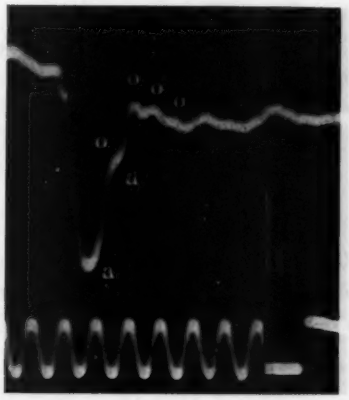


Fig. 7. ERG in the case of Oguchi's disease after 12 hours in dark.



In this ERG obtained after 12 hours in the dark, the a-wave and b-wave enlarged further. The a_1-wave was larger then a_2 in amplitude. Strangely enough, a_1 on the ascending limb of the b-wave became smaller compared with that of the case of after 3 hours dark adaptation.

Discussion

There are several reports on the ERG of Oguchi's disease. Hirose[4] observed ERGs in two cases of Oguchi's disease. His two cases lacked b-wave. Sato[8] reported that the ERG of one case of Oguchi's disease consisted only of a- and x-waves. There are some other reports bringing nearly the same results.

Thus, it has been concluded that the ERG of Oguchi's disease was composed only of the a- and x-waves, that is, photopic components.The ERG obtained after long term dark adaptation of this disease was first described by Nagata[7]. His case showed appearance of a positive b-wave after lengthy dark adaptation. He also observed that this positive b-wave was then recongnized only by the first light stimulus.

Recently Mizuguchi and Mase[6] reported the ERG in one case of this disease obtained after long term dark adaptation. He recongnized the appearance of b-wave and enlarging of a-wave after longer dark adaptation duration. He also reported that a_1 enlarged more than a_2 in amplitude during dark adaptation.

He presumed that in Oguchi's disease, some scotopic components were contained in a part of a_1-wave.

In my study some interesting facts were revealed concerning the amplitudes of a_1, and a_2-waves. The most interesting fact was the remarkable enlarging of a_1-wave, and diminishing of a_2-wave during dark adaptation, because the former is considered to belong to photopic mechanism and the latter, to scotopic mechanism.

Armington et al[1] maintained from their experiments with stimuli of different spectral composition and various conditions of dark adaptation that the earlier a-wave (a_1) was photopic and the later (a_2) was scotopic. But they did not deny the possibility that the "broken" appearance of a-wave might occur due to the genuine positive hump in the a-wave.

Thereafter E. Auerbach and Burian[2], dealing with ERGs after dark adaptation, reported that at the beginning of dark adaptation $a_1 > a_2$, and $x > b$, while at the later stages of adaptation $a_2 > a_1$, and $b > x$. From this fact they stated that both the first negative deflexion (a_1) and the first positive deflexion (x) appeared to belong to the photopic mechanism, whereas the second negative (a_2) and the second positive deflexion (b) to the scotopic mechanism.

Sanada[9] also presumed from his study on ERG of suckling albino rabbits, that a_1 and o_1 meant photopic response and a_2 and o_2 meant scotopic response.

We found it rather difficult to understand why in the ERG of Oguchi's disease a_1 which has been regarded as a photopic component, actually enalrged after dark adaptation and a_2, which has been regarded as scotopic, actually diminished.

Recently Bornschein and Goodmann[3] investigated ERGs of congenital night-blindness and color-blindness, and suggested that the "break" splitting a-wave into two portions (a_1 and a_2) might be genuine positive humps leading a series of later humps representing a type of oscillatory response.

Furthermore, Yonemura[10], studying these oscillatory potentials clinically and in many sorts of vertebrates, regarded this hump as a new component of ERG, and suggested that the oscillatory potentials are different from the conventional ERG in generation mechanism. He maintained that the splitting a-wave into a_1 and a_2 was caused by such oscillatory potentials.

Results of our recdnt study can be explained by these theories to some extent. It may be thought that in Oguchi's disease the a-wave composed of scotopic and phsopic mechanism enlarged after dark adaptation because of the scotopic mechanism. It is also natural for the scotopic b-wave to appear under these dark-adapted environments.

And it may be reasonable to presume that the apparantly enlargement of a_2 is due to the position of the first hump which happens to ride on the steep ascending limb of b-wave. The implicit time of humps in all these ERGs is the same.

Our recent conclusions seem to support the concept suggested by Bornschein & Goodmann and Yonemura. In another paper we are prepared to discuss this problem further in reference to another case of Oguchi's disease.

Summary

On a case of Oguchi's disease, ERG obtained after long term dark adaptation was investigated. On ERG obtained after 3 hours dark adaptation, a-wave enalrged and b-wave appeared. On ERG obtained

after 12 hours of dark adaptation, a and b enalrged further.

The amplitude of a_1 and a_2 was very interesting. The amplitude of a_1 remarkably enlarged with the duration of dark adaptation. However, a_2 was rather weakened.

The traditional theories cannot explain these facts, because they maintain that a_1 belongs to photopic mechanism and a_2 belongs to scotopic mechanism.

Our conlcusion seems to support the concest suggested by Yonemura and Bornschein et al.

REFERENCES

1. Armington, J.C., Johson, E.P. & Riggs, L.A.: J. Rhysiol., 118: 289, 1952.
2. Auerbach, E. & Burian, H.M.: Am. J. Opht., 40: 42, 1955.
3. Bornschein, H. & Goodman, G.: A.M.A. Arch. Opht., 58: 437, 1957.
4. Hirose, T., Acta O. Jap., 56: 732, 1952.
5. Jacobson, J.H.: Clinical Electroretinography. Springf., 125, 1961.
6. Mizuguchi, I. & Mase, T.: Acta O. Jap., 67: 1854 1963.
7. Nagata, M.: Acta O. Jap., 66: 1614, 1962.
8. Sato. K.: Acta O. Jap., 61: 1241, 1957.
9. Sanada, T.: Acta O. Jap., 66: 1430, 1962.
10. Yonemura, D.: Acta O. Jap., 66: 1566, 1962.

COMPARATIVE STUDIES ON THE RETINAL ARTERIOLAR AND THE RENAL ARTERIOLAR CHANGES IN HYPERTENSIVES, AS STUDIES BY MEANS OF OPHTHALMOSCOPY AND RENAL BIOPSY (REPORT I)

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It is indisputable that the ophthalmoscopic studies on the retinal vessels contribute very much to the clinico-pathological studies on the hypertensive disease of different sort. The anatomical peculiarity of the retinal vessels is that they belong to arterioles or venules according to their sizes and structures, and they can be observed opthalmoscopically without discomforting the patients. The aim of the ophthalmoscopy of the fundus in hypertension is to infer the vascular conditions of other organs in the body by means of the ophthalmoscopic findings in the retinal vessels.

Therefore the most important of the many eye-ground changes are those of the retinal arterioles.

Usually, the retinal arteriolar changes in hypertensives are divided into two kinds: the functional or hypertonic changes and the organic or arteriolosclerotic changes. It is sometimes difficult to divide these changes ophthalmoscopically and some changes have poor ophthalmoscopic-histological correlations; for example, narrowing and irregularity of the caliber of arteriole, anatomical structure of arteriovenous crossing, histological finding of reflex streaks of atrerioles, etc. These problems are under active study and some outcomes have been reported. It is difficult to obtain sufficient materials by which we can compare precisely the histological findings with ophthalmological findings. Under such conditions it is of some significance to compare the ophthalmoscopic changes of the retinal arterioles with changes in biopsy specimens of organs such as kidney. In this connection, it may be possible to find some correlation between histological changes and ophthalmoscopic observations.

In this article, the authors intend to discuss the relation between the ophthalmoscopic findings of the retinal arterioles and the histological findings of the kidney biopsy specimens of patients with hypertensive diseases.

Materials and Methods

Eye-ground changes and kidney biopsy specimens were studied on 30 patients including 27 hypertensives and 3 non-hypertensives who had ophthalmoscopically similar vascular manifestations. They were out- or in-patients of ophthalmological clinic of Hirosaki-University Hospital; each age, sex, blood pressure, duration of hypertension and other clinical data of the pateints are shown in Table I.

Table 1. Materials and clinical data.

Case	Sex	Age years	Blood pressure mmHg	Duration of Hypertension	Albuminuria	P.S.P at. 15%min.	N.P.N. mg/dl	Clinical diagnosis
1	M.	73	120/70	No	—		24.0	Chronic hepatitis
2	M.	57	136/70	Transient, 6 y. ago	—	20	36.5	Arteriosclerosis
3	F.	60	136/86	Transient 5 m. ago	+	25	34.0	Arteriosclerosis Autonomic ataxia
4	F.	25	140/89	210 systolic several m. ago	—	53	33.5	Essential hypertension
5	M.	34	146/90 (178/120)	One y.	—			Essential hypertension
6	M.	56	140/100	10y.	—	35	27.0	Essential hypertension
7	M.	70	180/ 82 (230/110)	—	—	35	27.0	Essential hypertension Arteriosclerosis
8	F.	58	140/ 80 (200/120)	—	±			Arteriosclerosis
9	F.	55	170/110	8 y.	—	45	36.5	Hypertension
10	F.	55	174/ 94	2 m.	—			Hypertension, Coronary insufficiency
11	M.	58	150/106 (180/120)	4 y.	—			Hypertension Arteriosclerosis
12	F.	51	140/ 90	—	—	35	32.0	Arteriosclerosis
13	M.	53	178/102	3 y.	—			s.o. Cerebromalacia
14	F.	55	170/100	15y.	++	30	32.5	Hypertension
15	M.	55	170/110	5 y.	—	25	34.0	Essential hypertension Cerebral arteriosclerosis
16	M.	58	150/ 94	3 y.	—		21.0	Hemiplegia Auricular fibrillation
17	F.	55	210/110	20y.	—	15	20.0	Hypertension Myocardial damage
18	M.	61	170/104	8 y.	—	5	36.0	Hypertension Heart insufficiency
19	F.	57	198/126	10m.	—	38		Hypertension Hypoplasia of the right kidney
20	M.	43	220/140	7 y.	±	22	32.5	Hypertension, Enlargement of left ventricle

21	M.	59	200/126 (150/ 96)	13y.	±		36.0	Nephrosclerosis (Chronic nephritis)
22	M.	30	150/110	3 m.	++	15	53.0	Chronic nephritis
23	M.	29	130/ 98	4 y.	++	10	72.4	Chronic nephritis Nephrosclerosis
24	M.	19	188/110	4 y.	±	25	72.0	Hypertension s.o. Chronic nephritis
25	M.	66	216/ 88	10y.	+++	15	59.5	Chronic nephritis
26	M.	32	130/ 80 (188/110)	—	—		62.5	Chronic nephritis
27	F.	52	220/110 (152/ 84)	—	+	8	56.0	Kimmelstiel-Wilson's syndrome
28	M.	59	164/100	—	—		38.0	Diabetes mellitus
29	M.	59	200/106	5 y.	—	20	33.5	Diabetes mellitus
30	F.	57	172/ 92	One y.	±	35	33.0	Diabetes mellitus

Fundi were examined closely by an ophthalmoscope of Neitz IIB after mydriasis. The findings were classified and graded according to Scheie's classification and recorded in films (SAKURA, ASA 50, Reversal) by means of Zeiss' fundus camera.

Kidney specimens were obtained from the patients by means of aspiration of biopsy with Vim-Silverman's needle and were fixed in 10 per cent formol, embedded in paraffin and stained with hematoxylin-eosin, then studied microscopically.

Results

Findings of ophthalmoscopy and kidney biopsy are summarized in Tables II and III.

Followings (Nos. 1, 2 and 3) are the normotensive cases with retinal changes ophthalmoscopically similar to those of hypertensives.

Case 1. A seventy-one year old man who had been treated for chronic hepatitis for one year. Liver biopsy showed the picture of chronic diffuse interstitial hepatitis. Blood pressure: 120/70, steady. Periarteritis of the retina was suspected ophthalmoscopically: renal biopsy showed senile atrophy.

Case 2. A farmer of fifty-seven was once noted to be slightly hypertensive six years ago, but not treated. His blood pressure was now 136/70 and constant. Only increased reflexes from the arterial walls was found in his eye-grounds and kidney findings were completely normal.

Table 2. Ophthalmoscopical findings.

Case No.	Arterioles Caliber	Arterioles Reflex	Arteriovenous Crossing Phenomena	Optik disk	Retinal changes	H	S	Ophthalmological diagnosis
1	Narrow, irregular	Increased with opaities	Absent	Normal	Hemorrhage, exudates	0	3	S.o. Periarteritis ret.
2	Normal	Increased	〃	〃	None	0	1?	Increasing of reflexes from arteriolar walls
3	Narrowed, irregular	Increased	Deviation, tapering		Hemorrhage	2	2	Arteriolosclerosis of the retina
4	Normal	Normal	Absent	〃	None	0	0	Fundus normalis
5	Narrow	Slightly increased	Absent	〃	None	1	0	Fundus hypertonicus

6	Slightly narrowed	Normal	Tapering	Normal	Hemorrhage	0	2	Arteriolosclerosis ret. Branchthrombosis
7	Narrowing, straightened	Increased, bright as a metal	Tapering#	〃	Hemorrhage	1	3	Arteriolosclerosis ret. Branchthrombosis
8	Narrow slightly	Increased	Tapering	〃	〃	1	2	〃
9	Narrow and irregular	〃	Tapering#	〃	〃	2	2	〃
10	〃	Slightly increased	Tapering	〃	〃	2	1	〃
11	Narrow, with caliber irregularity	Increased	Tapering of slight grade	〃	None	2	2	Arteriolosclerosis ret.
12	Narrow	Increased polish	?	〃	〃	1	2	Arteriolosclerosis, Intravitreal bleeding
13	Irregularly narrow	Increased	Deviation	〃	Hemorrhage	1	2	Arteriolosclerosis ret.
14	Narrow; caliber irregularity was marked	Increased, turbid	Deviation Tapering Banking	〃	None	2	3	〃
15	〃	Increased markedly	Tapering	〃	〃	2	2	〃
16	Narrowing; caliber irregularity	Increased, turbid	Deviation Tapering	Atrophic	〃	1	3	Arteriosclerosis ret. Optic atrophy (rt.)
17	Narrowing & caliber irregularity remarkable	Increased, opaque in part	Tapering	Atrophic	Hemorrhage	2	3	Arteriolosclerosis ret. Optic atrophy (both)
18	〃	Bright, some turbid	Deviation Tapering# Banking	Hypermic	Hemorrhage, white patches	2	3	Arteriolosclerosis ret. Ret. proliferans o.s.
19	Narrwing#	〃	Tapering	〃	〃	3	3	Arteriolosclerosis ret.
20	Narrow	Very increased	Deviation# Tapering#	〃	None	3	2	Fundus hypertonicus
21	Narrowed irregularly	Increased, turbid.	〃	〃	Hemorrhage, cotten-wool patches	3	3	Retinopathia hypertonica
22	Narrow	Increased	Absent	Normal	None	1	1	Fundus hypertonicus
23	Normal	Normal	〃	〃	〃	0	0	Fundus normalis
24	Narrowed, irregularly	Increased	〃	Hyperemic	〃	2	0	Fundus hypertonicus
25	〃	〃	Tapering	Normal	Hemorrhage, white spots	2	2	Retinopathia nephritica
26	Narrowed slightly	〃	Absent	〃	None	0	1	Arteriolosclerosis ret.
27	Markedly narrow	Increased much	Tapering	〃	Hemorrhage, white patches	3	3	Retinopathia diabetica
28	Narrow	Increased slightly	Tapering ?		None	1	1	Fundus hypertonicus
29	〃	Increased	Tapering Banking	〃	〃	2	2	Arteriolosclerosis ret.
30	Narrowed irregularly	〃	Banking# Tapering	〃	Hemorrnage, white spots	2	2	Arteriolosclerosis ret.

Case 3. A sixty-year-old housewife. Her blood pressure was 136/80, but its fluctuation had been pointed out five months before by another doctor and she had been treated for arteriosclerosis and autonomic ataxia. Eye-grounds; Arteriolar slcerosis with A/V crossings (taperings). Kidney biopsy: Arteriolar nephrosclerosis.

Table 3. Findings of kidney biopsy specimen

Case No.	Interlobular arteries	Arterioles	Glomeruli	Tubules	Interstitial	Histological diagnosis (Nephrosclerosis)
1	Thickening ±	Normal	Fibrosis & hyalinization slight	Normal	Normal	Senile atrophy
2	Thickening, hyalinosis	〃	Fibrosis ±	Casts ±	Fibrosis	Not pathologic
3	〃	Thickening, hyalinosis	Fibrosis	Dilation, atrophy, casts	Fibrosis	Nephrosclerosis
4	Normal	Normal	Normal	Normal	Normal	Normal
5	Normal	〃	〃	〃	〃	〃
6	Medial thickening of arcuate art.	〃	〃	〃	〃	No nephrosclerosis
7	Thickning of the wall of arcuate art.	Thickening of the wall	Hyalinosis	Dilation of lumina	Leucocytic aggregates	Nephrosclerosis
8	?	?	?	Marked dilation, atrophy, full of casts	Fibrosis	Nephrosclerosis ? ?
9	Thickening, hyalinosis	Thickened slightly	Fibrosis	Casts ± atrophy	Fibrosis ±	Arteriosclerotic nephrosclerosis
10	Thickening; hyalinosis of	?	?	Casts	Leucocytic infiltration	Nephrosclerosis
11	Thickening, hyalinosis; marked		Fibrosis, hyalinosis, adhesion hypercellualrity	〃	Fibrosis ±	Nephrosclerosis (of slight grade)
12	Thickened wall	Normal	Normal	Normal	Normal	?
13	Thickening±, hyalinosis	Marked thickening, less hyalinosis	Hypercellularity of the tuft	〃	Leucocytic infiltration	Nephrosclerosis (of slight grade)
14		Thickening of the wall	〃	Dilatiion, atrophy, casts	Fibrosis	〃
15	Thickening	Thickening	〃	Atrophy	Fibrosis ±	〃
16	?	Normal	Normal	Normal	Normal	No nephrosclerosis
17	Hyalinosis, marked thickening	Thickening, hyalinosis	Hyalinosis marked	Dilation, atrophy, casts	Fibrosis, infiltration of leucocytes	Nephrosclerosis (of high grade)
18	Thickening	Hyalinosis	Normal	Dilation	Leucocytic infiltration	Nephrosclerosis ?
19	Thickening; hyalinosis of slight grade	Thickening, hyalinosis	Hypercellualrity, adhesion	Dilation, atrophy, lots of casts	Normal	Nephrosclerosis
20	Thickening, Hyalinosis; of arcuate art. also	Thickening, hyalinosis	Fibrosis, hyalinosis, adhesion	Normal	Infiltration of leucocytes	Nephrosclerosis (of high grade)

21	Thickening, of arcuate art. also	〃	〃	Dilation, atrophy, casts	〃	〃 (secondary)
22	Thickening of the wall	Not determined	〃	Dilation	Fibrosis, hyalinosis, leucocytic infiltration	〃
23	Not determined	Marked thickening	Fibrosis, marked hyalinosis	Atrophy, Dilation	Fibrosis, infiltration of leucocytes	〃
24	Thickening, slight	Normal	Hypercellarity, adhesion	Normal	Normal	Chronic glomerulonephritis
25	Thickening, hyalinosis	Thickening, hyalinosis	Fibrosis, hyalinosis	Dilation, casts	Leucocytic infiltration	Nephrosclerosis
26	Arcuate art, too	〃	Fibrosis adhesion	〃	Fibrosis, slight	Chronic glomerulo-nephritis Nephrosclerosis
27	Thickening, hyalinosis	Marked thickening, hyalinosis	Hyalinosis ⫴ nodular lesion	Atrophy ⫴ Dilation	Fibrosis, hyalinosis, infiltration of leucocytes	Diabetic nephrosclerosis
28	Normal	Normal	Fibrosis, Hypercellularity	Normal	Hyalinosis	Normal
29	Thickening, fibrosis	Hyalinosis, thickening	Hyalinosis adhesion, hypercellularity	Dilation	Fibrosis ⫲ Hyalinosis	Nephrosclerosis
30	〃	Hyalinosis	〃	Atrophy, casts ⫲	Fibrosis, hyalinosis, leucocytic infiltration	Nephrosclerosis

The next two (Nos. 4 and 5) are thought to be cases of the early stages of essential hypertension with episodic palpitation, headaches and high blood pressure. In their eye-ground, arteriolar sclerotic changes were not observed, while hypertensive changes were absent in one case and very slight in the other. No lesions were found in kidney specimens.

Cases Nos. from 6 to 10 were patients with essential hypertension who had sclerotic changes in the ocular fundi, accompanied by occlusion of the branch of the retinal central veins. Among these five cases, one (No. 6) had no sign of nephrosclerosis including arteriolar change, and two (Nos. 7 and 9) had some findings of nephrosclerosis. In the other two (Nos. 8 and 10),arterioler changes in the kidney were not clarified, because the number of glomeruli and arterioles was too small to diagnose the changes, but nephrosclerosis was suspected from the changes in the tubules.

Case 6. A fifty-six year old farmer has suffered from occasional head-aches and high blood pressure for about 10 years. His blood pressure was 140/100 and stable. Ophthalmoscopically, arteriosclerotic changes were found but no hypertensive changes. In his kidney, intimal proliferation was found in one of the arcuate arteries, but there were no other pahtological changes in the specimen (Fig. 1, 2).

Case 7. A seventy year old male. He came to our clinic compalaining of visual disturbance in his right eye, which was due to occlusion of the retinal veins. His blood pressure was discovered to be 230/110. Under treatment it fell to 180/82 several weeks later. By ophthalmoscopy narrowing and straightening tendency and increased reflex stripes of the arterioles together with and crossing phenomena were found. Also kidney biopsy showed changes of benign nephrosclerosis.

In the next eleven cases of essential hypertension (Nos. 10 to 20), there were found arteriolosclerotic

changes but no venous occlusisons in their retina. By kidney biopsy, eight cases showed arteriolar changes, while two (Nos. 12, 16) revealed very slight changes if any (Fig. 2,3).

Case 16. A fifty-eight year old male. He consulted for impairment of vision in his right eye and palsy of the left extremities which had occured three years ago. Ophthalmological diagnosis was optic atrophy of the right eye and arteriosclerosis of the retina. Though the retinal arterioles were narrowed by the irregularities of caliber and turbidity of the walls, kidney biopsy did not reveal any lesion (Fig. 5, 6).

Case 17. A fifty-five year old female. Since she was thirty-three, her systolic blood pressure had been 160 or more and she had been treated intermittently. At the age of fifty-three she suffered from diplopia due to ophthalmoplegia totalis o. dextra. Several months later atrophy of both eyes occured. Her blood pressure fluctuated between 210/110 and 170/90. No albuminuria was found. E.C.G. revealed myocardial damage. Retinal arteries were narrowed and covered with white sheaths, accompanied by increased reflexes and opacities of the walls. Arterio-venous crossing phenomena were also observed. Kidney biopsy showed pronounced thickening, hyalinization and fibrosis of the glomeruli and arterioles. Small arteries of the interestitial tissues were thickened and hyalinized. Lymphocytic infiltrations were found in the interstitial tissue (Fig. 7, 8).

Case 20. A fourty-three year old male. He had been noticed of hypertension seven years ago but had not consulted for treatment. His blood pressure was 230/140. Slight albuminuria was found but the sediment was normal. Roentogenologic examination indicated enlargement of the left ventricle and electrocardiogram showed myocardial damage. PSP test: 20 per cent at 15 minutes and 70 per cent at 120 minutes. Cholesterol, sodium and potassium in the serum were normal. Ophthalmoscopy revealed remarkable hypertensive changes together with sclerotic changes and hyperemia and blurring of the optic disks. Because of these findins it was suspected that a benign hypertension was converting to a malignant stage. Renal biopsy specimen revealed a picture of benign nephrosclerosis; there was no arteriolar necrosis (Fig. 9, 10).

Six following, Nos. 21 to 26, illustrate the cases of hypertension of renal origin. Four of these six cases had nephrosclerosis.

Case 21. A fifty-nine year old male. He camplained of impairment of vision in his left eye. His right eye was blind due to occlusion of the central retinal vein complicated by hemorrhagic glaucoma since the age of fourty-six. His blood pressure was 200/106, and albuminuria of slight grade was found. Ophthalmoscopical findings such as sclerotic changes with hypertensive changes of the arterioles, blurring of the optic disk (without papilledema), presence of cotton-wool patches and hemorrhagic spots, made the authors suspect that this was a case of malignant hypertension in its early stage. But it was known that he had been suffering from chronic nephritis at the age of twenty-one and had been treated for three years. Since his age of fourty-six, high blood pressure was sometimes noticed and it fluctuated between 170 and 200 systolic and 120 and 130 diastolic. Six years ago he was admitted for treatment of hypertension with myocardial damage and disturbance of renal function, and his blood pressure dropped to 140/92. Histological findings in the kidney revealed hypercellularity in the glomerular capillaries, adhesions of the glomerular tufts with Bowman's capsules, the latter were thickened and some of the glomeruli

Fig. 1. Fundus of Case 6 (56 year old male; essential hypertension). Retinal hemorrhages and white spots due to thrombosis of the superior temporal vein. Irregularities of caliber of retinal arterioles and arteriovenous crossing change of slight grade are shown.

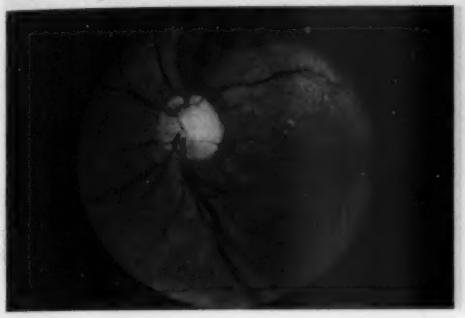


Fig. 2. Renal biopsy of the same case showing intimal proliferation of an arcuate artery.

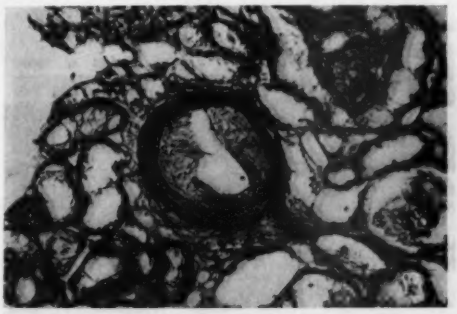


Fig. 3. Fundus of Case 7 (70 year old male; essential hypertension). Thrombosis of the superior temporal vein. Narrowing and straightening of ateriole accompanied by increased reflex and tapering of high grade.

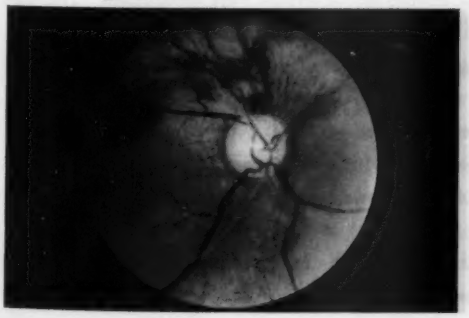


Fig. 4. Renal specimen of the same case. Thickening of an interlobular artery and an afferent arteriole.

Fig. 5. Eye-ground of Case 16 (58 year old male; essential hypertension with left hemiplegia). Optic atrophy, narrowing and irregularities of caliber of the inferior temporal artery with opacities of the wall.

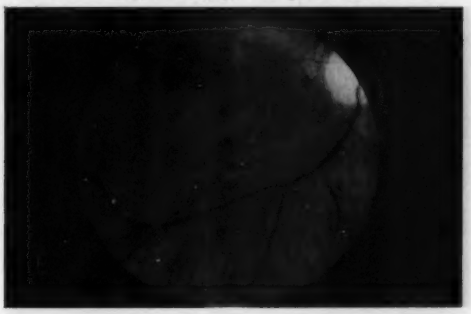


Fig. 6. Kidney biopsy of Case 16 shows no abnormality.

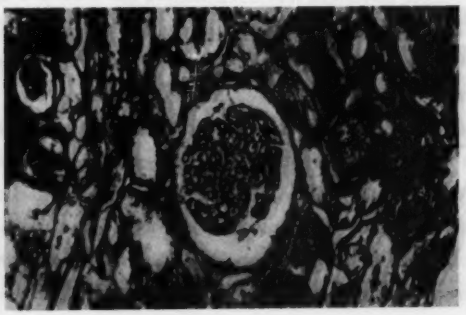


Fig. 7. Fundus of Case 17 (55 year old female; essential hypertension). Optic disk is pale. Narrowing and caliber-irregularities of the retinal arterioles are prominent. Arteriolar white sheathing and arteriovenous crossing signs of high grade are also found.

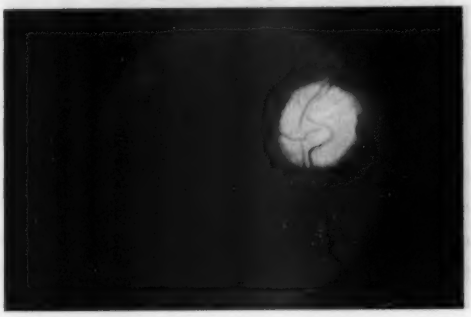


Fig. 8. Thickening and hyalinosis of smaller retinal arteries and Bowman's capsule associated with collection of lymphocytes in interstitial tissue, from the same case. Retention of urine in tubules and hyalinized glomeruli.

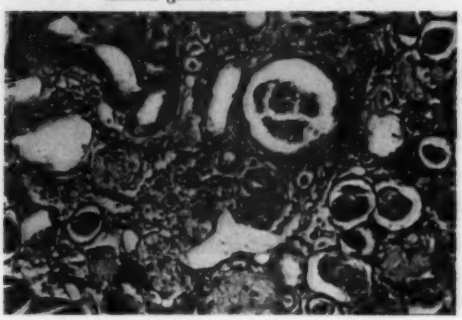


Fig. 9. Case 20 (43 year old male; essential hypertension). Ophthalmoscopy reveals hyperemia and turbidity of the optic disk, narrowing and tortuosity of a retinal artery, Guist's phenomena, and crossing signs.

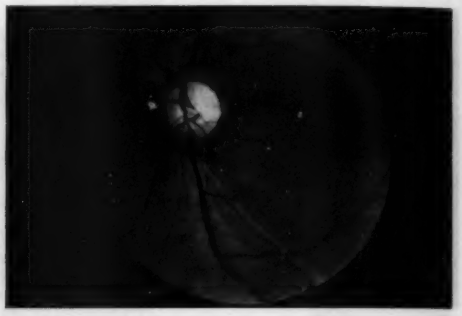
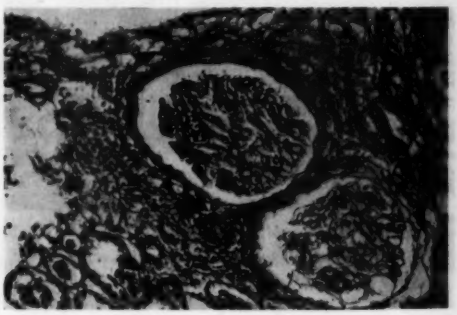


Fig. 10. Renal biopsy from the same case. Accumulation of lymphocytes around glomeruli and fibrosis of interstitial tissue. Slight dilation of the lumen of some tubules.



were entirely hyalinized. Infiltration of lympocytes in the interstitial tissues was pronounced. As to the vessels, haylinosis and thickening of the walls of small arteries and arterioles were recognized. Therefore the case was thought to be secondary nephrosclerosis caused by chronic nephritis (Fig. 11, 12, 13).

In the kidney of case No. 23, histological findings of nephrosclerosis were found, although there were no pathological changes in the eye-grounds.

Four cases of hypertension with diabetes mellitus were also studied.

No. 27, a fifty-two year old female of diabetic retinopathy, revealed higher hypertensive or sclerotic changes of the arterioles in the retina and remarkable nephrosclerosis including nodular lesion of glomerular tufts in the kidney.

In the last two cases (Nos. 29, 30) with sclerotic changes of the retinal arterioles, kidney specimens revealed signs of nephrosclerosis but no nodular lesions. There was one case (No. 28) who did not have

Fig. 11. Fundus of Case 21 (59 year old male; chronic nephritis). Optic disk appears somewhat edematous with hyperemia and opacities. Retinal arterioles are narrowed and of irregular caliber. Tortuosities of venules, hemorrhages and cotton-wool white patches are noticed in the same case.

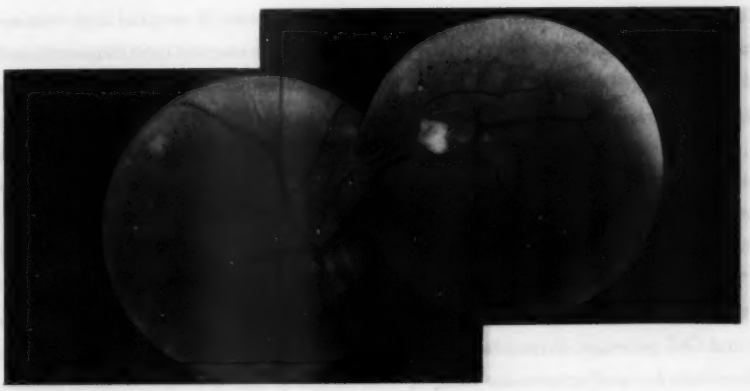
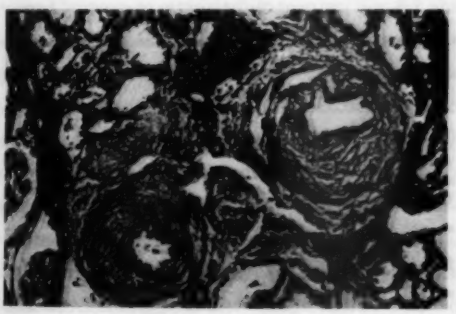


Fig. 12 and 13. Renal changes in the same case. Hyalinosis of glomerulus. thickening and fibrosis of the walls of arcuate arteries, and lymphocytic aggregates surrounding them are shown in Fig. 12. Hypertrophy and hyalinosis of an afferent arteriole and Bowman's capsule, and an increased cellularity of glomerular capillaries found in Fig. 13.



nephrosclerosis, and had hypertensive but not sclerotic changes in the eye-grounds whose glycosuria was controlled easily by dietary management.

Comment

One of the reasons for studying renal biopsies, in spite of many previous excellent studies in this field, was that we were interested in the role of the kidney in hypertensive disease, especially in differentiation of benign and malignant hypertension. The authors have not dealt with a case of essential hypertension of Keith-Wagener's Group II which developed to Group III, and have doubted the existence of such a case.

In view of the kidneys role in the etiology and pathology of hypertensive diseases, it has been studied for a long time by many authors. It is recognized that there may occur sclerotic changes in the entire arteriolar system in the patient of hypertension, especially in the arterioles of the kidney in case of essential

hypertension, although there are still some discussions whether the kidney participates in the mechanism of hypertension primarily or not; namely,whether the arteriolosclerosis is the cause or the effect of essential hypertension.

According to the patholgical study by Fujii[1,2,3,4] on the patient of essential hypettension including 36 cases of benigh type and 14 of malignant type, arteriolar sclerosis occurs most frequently in the kidney. He classified the changes of arterioles in hypertensives into four groups; (1) intimal thickening, (2) hypertrophy of muscular layer, (3) intimal hyalinosis and (4) fatty degeneration of the intima. And he considered that only (4) is the true manifestation of arteriolosclerosis, Fishberg[5] also found arteriolar lesions in the kidney of all cases of 72 patients with essential hypertension. Mukae[6] classified the thickenings of the arteriolar wall into four types: (A) simple thickening, (B) fibrinous hyaline thickening, (C) fibrinous necrotic hyaline thickening and (D) necrotic hyaline thickening. And he stated that the third one (C) is the most essential of the changes of the arterioles in the hypertension, and it is found more frequently in the kidney than in the other organs.

Moritz and Olt[7] presented three basic lesions of arterioles in hypertension; (1) intimal hylinization (2) medial hypertrophy anddegeneration and (3) intimal proliferation. They considered that arteriolar sclerosis is more likely the cause than the effect of hypertension. Afterwards, however, another opinion was brought by the study of Castleman and Smithwick[8,9] by means of renal biopsy specimens from patients with essential hypertension. Castleman and Smithwick thought that hypertension precedes the organic changes (arteriolosclerosis) of the renal arterioles, because 4.2 to 7 per cent of their cases of essential hypertension had no or slight evidence of arteriolar sclerosis. Heptinstall[10] supported this opinion by his renal biopsy studies. The examination of kidney biopsy specimens from 1350 patients with hypertension made Sommers et al[10] conclude that renal ischemia precedes detectable vascular abnormalities in essential hypertension. When organic changes have developed in the arteriolar walls, secondary renal changes may serve to maintain or accelarate the process of the disease. These authors reported that the higher became the diastolic blood pressure the more advanced were the sclerotic changes of renal arterioles.

The sclerotic changes were thickening and hylainosis of the walls, which were found in the arterioles in our kidney specimens stained with hematoxylin-eosin although 6 of 27 cases of hypertension had no such evidence in the renal arterioles (Nos. 4, 5, 6, 16, 34, 28). Two of them were thought to be the cases of essential hypertension in its early stage (Keith-Wagener's Group I) and two others were those of hypertension of some duration. According to Sommers et al, cloudy swelling, dilation and atrophy of some convoluted tubules and accompanying spasm of afferent arterioles were the earliest alterations observed; intramural edema and muscular hypertrophy occurred subsequent to spastic arteriolar contraction; then these changes were followed by arteriolar elastic tissue degeneration and hyalinization in afferent arterioles. In the more advanced stage of arteriolosclerosis scars, lymphocytic aggregates in interstitial tissue and glomerular alterations may occur. In the majority of our cases, the changes found most frequently, were enlargement and atrophy of the convoluted tubules. These changes have been described hitherto as one of the microscopic signs of nephrosclerosis in text books of pathology, but it is likely that they may occur in early stages of hypertension before arteriolosclerotic changes appear, as Sommers et al reported. Lymphocytic infiltrations in interstitial tissue were considered to be the reparative reaction to the tubular atrophy; they were found in 11 cases, most of which were accompanied by renal arteriolar sclerosis and glomer-

ular hyalinosis of higher grade.

Concerning arteriolar necrosis or necrotizing arteriolitis which has been regarded as one of the pathognomonic changes of malignant nephrosclerosis since Fahr[12] first pointed it out, it was not found in any of our cases. Accorcing to Castleman and Smithwick, there was no case of necrotizing arteriolitis in 100 hypertensives including 14 cases of malignant hypertension. This result differs from that of Fahr and others who did post-mortem examinations. On the other hand, studying renal biopsy specimens, Sommers states that necrosis of arterioles may occur in any stage of arteriolosclerosis and it can have some relation to malignant hypertension but cannot be the synonym of it. Schroeder[13] pointed out, also, that this change develops with rare exceptions only in the presence of azotemia and he advocated the necessity of differentiation between the pathological and clinical diagnosis. The authors are in agreement with Schroeder's opinion; we think that one must differentiate between the pathological and clinical diagnosis of nephrosclerosis, especially, of malignent nephrosclerosis.

In regard to the relation of histological changes of kidney to that of the retina, Hiwatari's[14] postmortem examination of about 57 hypertensives who died at the ages of 60 and more revealed no intimate correlation between them as to arteriolosclerosis, and he reported no or slight arteriolar sclerosis in the majority of the kidney despite the existence of marked sclerotic changes in the retinal arterioles. Meanwhile Fujii reported of essential hypertension that arteriosclerosis of the kidney was observed in 95 per cent cases and of the choroid 75 per cent, but of the retina in less than 6 per cent histologically. According to Castleman et al, there was some relation between eye-ground changes and renal biopsy specimens, especially in the extremely low and high grades. The authors found a case (Case 16) in which ophthalmoscopical changes preceded those of renal biopsy, though in the majority the tendency was as reported by Castleman et al. Saltz[15] et al thought that the discrepancy between them concerning the grade of arteriolar changes in hypertension is essentially due to focality and irregualrity of the occurrence of lesions in its early stage, and this was supported by the fact that there are sclerotic changes of various degrees even in one retina as we can recognize ophthalmoscopically and as Wagner-Clay-Gipner or Kato[16] et al described. However we must also give consideration to the peculiarity of the reaction of each organ to arteriolar hypertension and sclerosis as Fujii, Fishberg and others observed and to the differences of the fundamental structure between the arterioles of the retina and those of the other organs, as pointed out recently by Ikui[17] and his coworkers.

Summary

The authors studied the relation between the ophthalmoscopical changes of the retinal arterioles and the histological findings of the kidney biposy specimens. Examinations were made on thirty patients, 27 cases of which were hypertensives and remaining 3 cases were non-hypertensives who had similar vascular manifestation in the eye to those of hypertensives.

Kidney specimens were gained by means of aspiration biopsy, fixed in 10% formol, embedded in paraffin and examined microscopically under hematoxylin and eosin staining.

1) Of 27 hypertensives renal arteriolar sclerosis was absent in 6 and present in the other 21 cases. There were six cases of advanced nephrosclerosis.

2) There was some correlation between the severity of the renal arteriolar changes and the ophthal-

moscopic findings of the retinal arterioles with some exceptions.

3) In these series there were no cases of measurable papilledema but 5 cases with hyperemia and opacity of the optic disks were observed. And arteriolar necrosis was not found in any case, although two of the patients possibly had malignant hypertension (Keith-Wagener's Group III).

4) Nephrosclerosis was found in 5 of 6 cases of renal hypertension. Crescent formation in the glomeruli was not recognized.

5) Out of four patients with hypertension and diabetes mellitus three had arteriolar sclerosis in the kidney but the typical nodular lesions of glomerular capillaries were found only in one case, which also had diabetic retinopathy.

REFERENCES

1. Fujii, S.: Acta Path. Jap., 14: 356, 1924
2. Fujii, S.: idem 15: 209, 1926
3. Fujii, S.: idem 16: 419, 1927
4. Fujii, S.: J. C. O., 9: 647, 1955
5. Fishberg, A.M.: Arch. of Internal med., 35: 650, 1925
6. Mukae, H.: Nagasaki Medical Journal, 35: 140, 1958
7. Moritz, A.R. & Olt, M.R.: Am. J. Pathol, 13: 679, 1937
8. Castleman, B. & Smithwick, R.H.: JAMA 121: 1256, 1943
9. Castleman, B. & Smithwick, R.H.: New England J. Med., 239: 729, 1948
10. Heptinstall, R.H.: Brit. Heart J., 16: 133, 1954
11. Sommers, S., Pelman, A. & Smithwick, R.H.: Am. J. of Pathol., 34(II): 685, 1958
12. Fahr, Th.: Virchows Arch. f. Path. Anat. u. Physiol., 226: 119, 1919
13. Schroeder, H.A.: Essential Hypertension, Berlin, Springer-Verlag, 1960, P. 238
14. Hiwatari, S.: Acta O. Jap., 57: 479. 1953
15. Saltz, M., Sommers, S. & Smithwick, R.H.: Circulation, 16: 207, 1957
16. Kato, K. et al: Acta O. Jap., 68: 1562, 1964
17. Ikui, H.: Acta O. Jap., 67: 562, 1963

ANGULAR DISTRIBUTION OF THE LIGHT SCATTERED FROM THE CLOUDED CORNEA

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Introduction

Transparency of the cornea is maintained by the lattice of collagen fibrils in the stroma, and the clouding is caused by the disturvance in the lattice structure.

Distribution of the scattered light is considered to be closely related to the state of deformation of fibril lattice and specific to the cause of the corneal clouding.

The purpose of the present work is to clarify the relationship between the distribution of the scattered light and the state of corneal clouding.

Method and Material

The bovine corneas were used within 2–5 hr after slaughter. The clouded materials of the corneas were

prepared as follows: The 6mm square piece was excised from the central area of the cornea whose epithelium and endothelium were removed. (a) The square piece was then immersed in 1% NaCl solution for 10 min-5 hr. The swollen and clouded stroma was obtained. (b) The square piece was immersed in the acetic acid buffer, pH 3–4, to which 2% chondroitin sulfate solution was added to prevent the cornea froms welling. The clouded stroma of approximately normal thickness was obtained.

(c) The excised normal cornea was immersed in 2% chondroitin sulfate solution for 10 min; no NaCl solution being added. The square piece was excised from this cornea. The epithelium of this preparation was cloudly, while the stroma was kept in approximately normal hydration and transparent.

(d) The corneal surface of the enucleated whole eye was dipped into the 2% acetic acid solution for 1 min, it was then washed with distilled water. The square piece was cut from this cornea. The stroma was kept in transparent, while the epithelium was cloudy.

The priciple of measurement of the scattered light was the same as described by Kikkawa 1960. The corneal piece was held between two pieces of glass plate and placed in the center of the rotating table, on which a photomultimplier tube was fixed. The parallel beam of light struck perpendicularly on the cornea. On rotating the table, the scattered light was measured in the range of 0°–177°. The P.D. across the 20KΩ resistor was measured with a vacuum tube voltmeter. The reading was proportional to the internsity of the scattered light. Ratio of the intensity of the scattered light/incidnet light was plotted against the scattering angles.

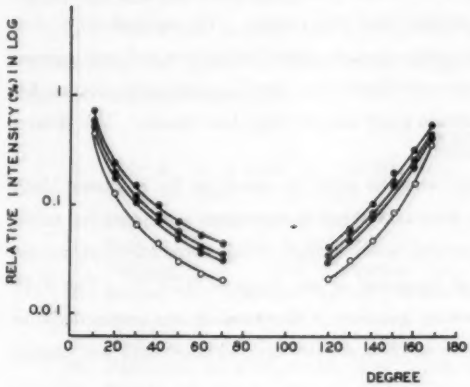
Another type of measuring apparatus was also used. The cornea was placed in the center of the rotating arm of long radius. A lens of long focal length was placed between the cornea and the light source, near the center of rotating arm. A system of diaphragms was put in the optical pathway. The convergent light, in place of parallel beam, struck the cornea. The image of the slit of light source was forcused through the cornea on the surface of the window of the photomultiplier tube. The very sharp image was forcused when the cornea was transparent. Since the radius of rotation of the arm was long, this apparatus made it possible to analyze more acurately the scattering in the narrow angles, less than 10°. The aperture of the window of the photomultiplier tube to the center of the rotating arm, i.e. to the cornea was 4′.

The relationship between the degree of clouding and the disturbance of visual acuity was investigated. The corneal piece was held between two glass plates and put in front of the eye. The visual acuity was tested through an artificial pupil of 2 mm diameter.

Results

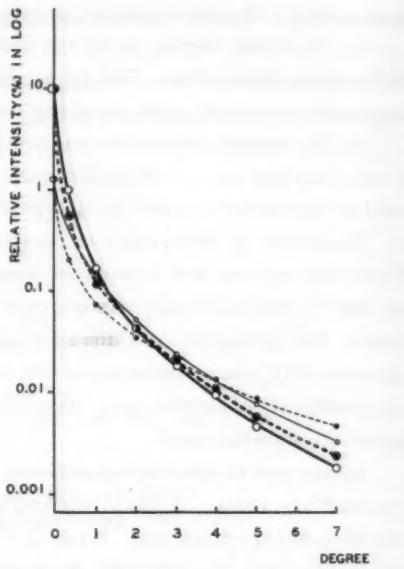
Fig. 1 shows some examples of the angular distribution of the scattered light of the clouded corneas. All the clouded materials given in this figure have approximately the same intensity of transmission (0°-direction). The scattering from the swollen stroma was smaller than that from the other kinds of clouded materials in the range of 10°-177°. However, the swollen stroma disturved the visual acuity mores eriously than the others, that is, the visual acuity was 0.1 when tested through the above mentioned swollen stroma, 0.6 through the acid treated stroma, and 0.5 through the cornea with clouded eipthelium. On the other hand, it was found that the scattering in the narrow angles, 0°-5°, was greatest in the case of swollen stroma (not shown in the figure). The precise analysis of narrow angle scattering was done by the use of a measuring apparatus of longer radius of rotation. Fig. 2 shows that the sacttering from the swollen stroma was greater than that from the acid treated stroma in the range of very narrow angles. (The

Fig. 1 Augular distribution of the scattered light.
○-swollen stroma, visual acuity 0.2
●-acid treated stroma, visual acuity 0.6
⊙-acid treated epithelium, visual acuity 0.6
◎-chondroitin treated epithelium, visual-acuity 0.5



These preparations have the equal intensity of trasmission. The scattering less than 10° is not shown in the figure.

Fig. 2. Narrow angle scattering of the clouded stroma.
○-swollen stroma
●-acid treated stroma



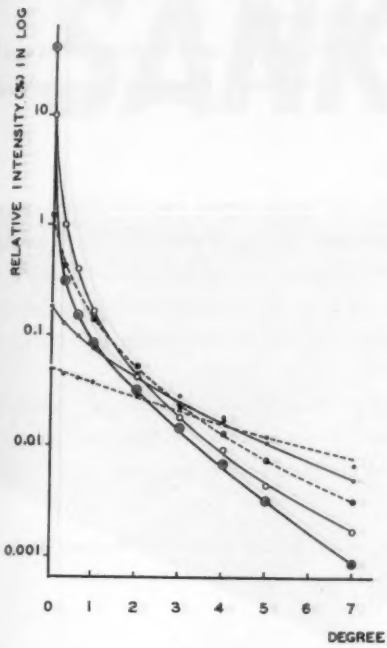
The swollen stroma and the acid treated stroma of equal intensity of transmission are compared. The scattering curves intersect each other. Two sets of experiments are given in the figure.

materials of equal intensity of transmission were compared). The scattering curve of the swollen stroma intersected with that of the acid treated stroma. The behaviour of the other kinds of clouded materials was similar to that of the acid treated stroma. (not shown in the figure to simplify the figure).

These facts lead to the concept that the disturbance of visual acuity mainly depends on the sacttering in the narrow angles. This relationship was found to be valid in the cases of clouded corneas of another intensity of transmission. Moreover, this concept was valid when the clouded corneas of different transmission were compared. An example will be shown on the swollen stroma. Fig. 3 shows the angular distribution of the scattered light from the swollen stromas of different transmission. It is generally known that the visual acuity does not depend on the absolute value of the intensity of transmitted light except an extreme dark condition; a neutral filter which attenuated the transmitted light by 3–4 times did not disturb the visual acuity. On this ground, Fig. 3 was redrawn; the scattered light was represented as % of the intensity of transmission in place of the incident light intensity. As the narrow angle scattering increased, the visual acuity was found to be correspondingly disturbed.

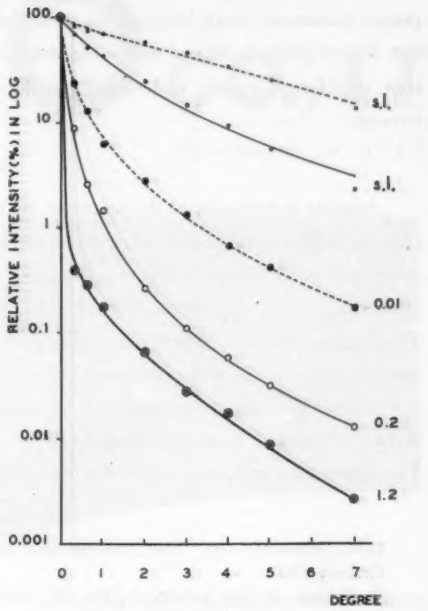
In order to know the characteristics of the scattering, the intensity ratio of the forward scattering/backward scattering was estimated, the intensity in the direction of 10° and 170° being taken arbitrary.

Fig. 3 Narrow angle scattering of the swollen stromas of different intensities of transmission.



For the sake of comparison, scattering of the transparent cornea (◎) is given.

Fig. 4. Narrow angle scattering of the swollen stromas, represented as % of the respective intensity of transmission.



Visual acuity is given on the right side of the curve.

◎-normal transparent cornea.

It ranged from 4 to 11 and in most cases of the clouded corneas it was 5–8. However, it was difficult to find a close relationship between the scattering ratio and the degree of disturbance of visual acuity.

Discussion

Maurice(1960)stated "The transparency of the cornea depends on the order of the fibrils in the stroma, any action which destroy the order will cause it to lose its clarity." "The clouding occurs when the cornea swells or is subjected to a mechanical stress. When the cornea swells, the rows of fibrils will become separated from one another. Each row will then lose its straightness since its individual members are pushing away from each other and the aligning forces of neighbouring rows are weakened." Many factors other than swelling or mechanical stress might destroy the order of fibrils in different and specific manner, and the scattering distribution might be specific to the causes of clouding. The present experiment showed that the distribution of the scattered light, especially from the clouded stroma, were specific to their causes of clouding.

The molecular dimensions are determined by measuring the scattering ratio, forward 45°/backward 135°, of the diluted solution of high polymers. While, the corneal stroma which is consisted of collagen fibrils is far apart from the dilute solution of high polymers. There is no theoretical background to

determine the characteristics of the lattice disorder by measuring the scattering ratio of the corneal stroma. In the present work, it was attempted, from the experimental view point, to determine the relationship between the scattering ratio and the causes of clouding. However, it has not been successful to find the proper parameter which indicates the characteristics of the lattice disorder.

Visual acuity is defined as the reciprocal of the angle subtended by the smallest detail which can be seen, therefore it is easily understood that the scattering in the narrow angles disturbed the visual acuity seriously.

Summary

Angular distribution of the scattered light from the clouded bovine cornea was determined using a photomultiplier tube and a vacuum tube voltmeter. The swollen stroma scattered the incident light exclusively in the narrow angles of propagation, accompanied with a slight scattering in the other directions. In contrast to this, the stroma treated with acetic acid and the cornea whose epithelium was treated with acetic acid or with 2% chondroitin sulfate scattered light rather slightly in the narrow angles of propagation and markedly in the other directions.

Visual disturbance was estimated by reading the test chart through the clouded cornea. Visual disturbance increased as the scattering from the cornea increased in the forward and backward directions. The degree of visual disturbance was particularly related to the narrow angle scattering.

REFERENCES

D.M. Maurice,: in "The Transparency of the Cornea" edited by Duke-Elder and Perkins, Blackwell, Oxford, 1960.

Y. Kikkawa: Jap. J. Physiol., 10: 292, 1960.

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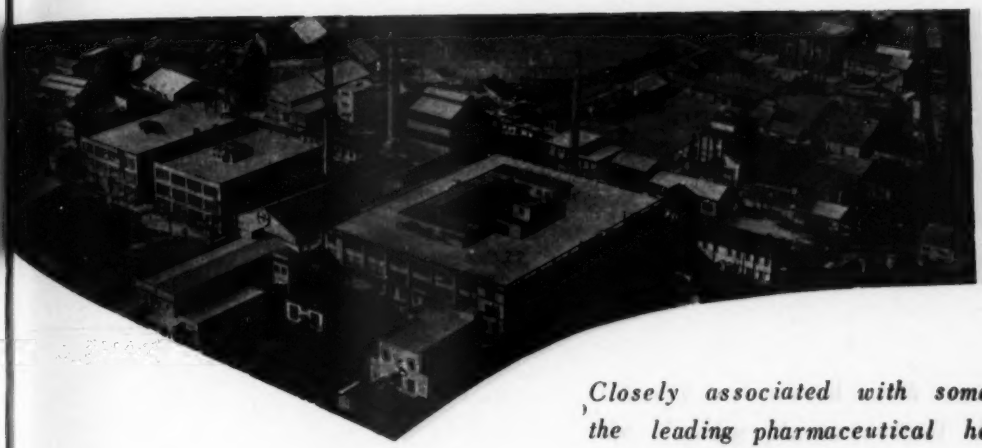

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